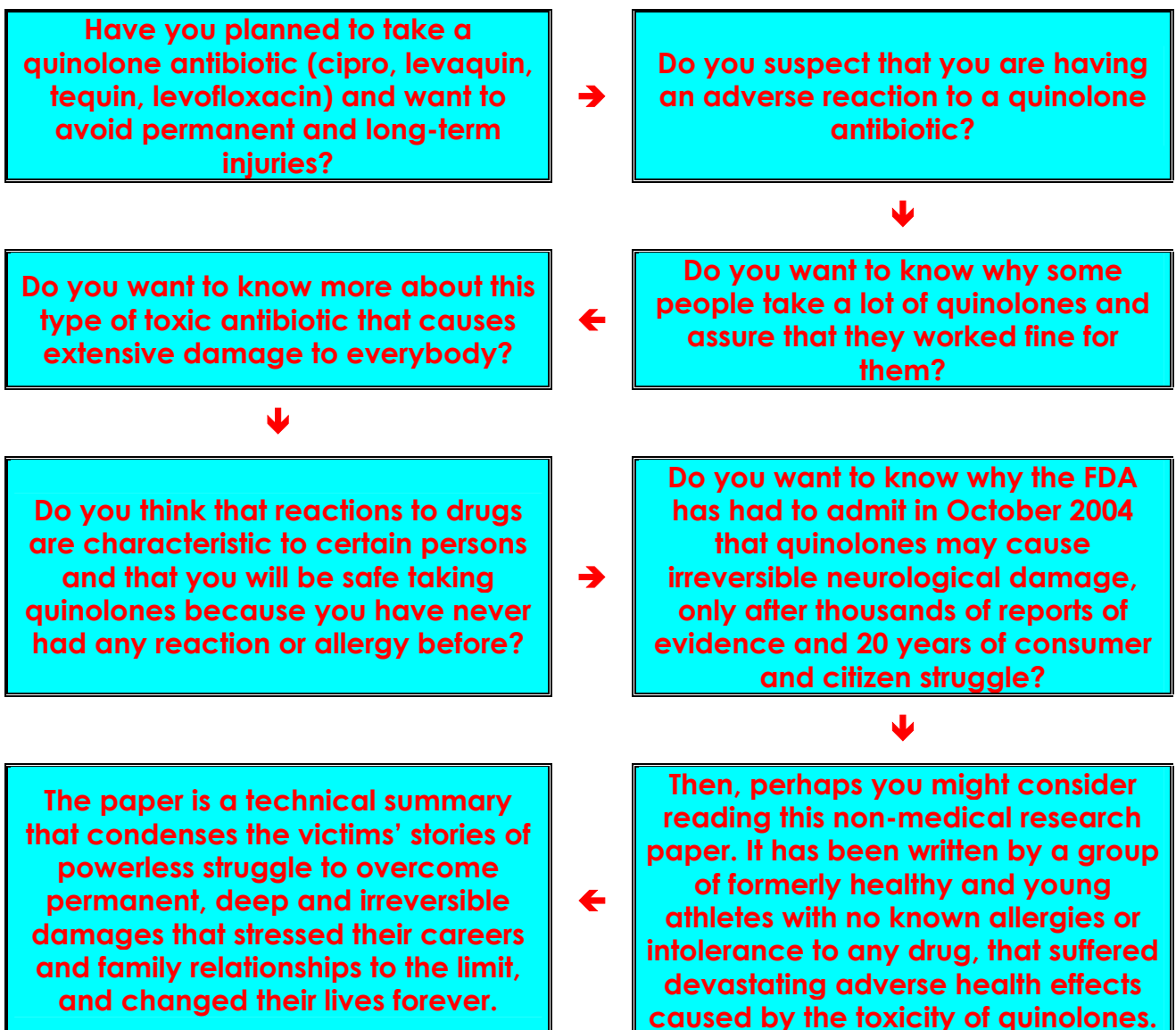


QUINOLONE ANTIBIOTICS TOXICITY



QUINOLONE ANTIBIOTICS TOXICITY A SUMMARY OF CLOSELY FOLLOWED CASES

Damage and disorders caused by quinolone antibiotics (cipro, levaquin, tequin and others).

**[QUINOLONES ARE A CLASS OF ANTIBIOTICS THAT ARE VERY TOXIC
FOR TENDONS, CARTILAGES, THE NERVOUS SYSTEM AND OTHER ORGANS]**

Last update: July 2005

WARNING.

This article consists of the description of the adverse toxic effects caused by the fluoroquinolone class of antibiotics, on previously healthy people. Many of those lesions are irreversible and permanent in nature. In addition, the article contains data obtained from many individual experiences, as well as information that comes from reputed medical sources available to the public. This article does not contain medical advice or professional statements on its own.

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AUTHOR.

Primarily T. Boomer, who has no professional medical background, has prepared the article and it is based on many personal experiences. The author of this study has no interest of any kind in any commercial activity, benefit or product related with the topic.

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Comments are welcome at: drugs2008@yahoo.com

- Our aim is to help stoping this useless wasting of lifes of innocent people -

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NOT TREATED IN THIS PAPER: MENTAL ALTERATIONS CAUSED BY QUINOLONE ANTIBIOTICS

Real damage of the mental functions

The quinolone and fluoroquinolone antibiotics act very hard on the central nervous system, causing very frequently a vast number of brain lesions and dysfunctions that cause mental alterations, and psychiatric states that can be debilitating and life altering both for the patient and the persons close to him/her. The present version of this paper does not deal with those serious events. Unfortunately, by leaving apart the psychological toxicity of the quinolones, the scope of this paper misses at least half of the toxic profile of this class of antibiotics. In some passages of the report certain mentions to them are made but they are not discussed in detail.

Among the most common injuries of this kind are the following (all of them listed in the package insert of a typical quinolone):

- depersonalization, depression paranoia, toxic psychosis, unresponsiveness, phobia
- restlessness, nervousness, dizziness, agitation, confusion, delirium, depression
- nightmares, hallucinations, manic reaction, irritability, anxiety, lethargy
- convulsive seizures, panic attacks, suicidal behaviour
- lightheadedness, vertigo, insomnia

Some persons have acquired very long lasting mental injuries after a single pill of levaquin, floxin, ciprofloxacin and other quinolones, not to mention the countless cases of tragic events caused by altered behaviours after the ingestion of quinolones, nearly all of which are blamed on to something else by the medical class.

Fictional diagnoses

Sooner or later, people affected by severe quinolone reactions are sent by their doctors to the psychiatrist. In many cases, these psychiatrists give the patient wrong diagnoses. The most common is paranoid delirium, by which the victim of the intoxication by quinolones sees symptoms and houses worries about the lesions suffered that only exist in his/her mind, simply because the psychiatrist firmly believes that an antibiotic cannot cause those long lasting arrhythmias, insomnia, joint pains, need of a walking aid or wheelchair, vision problems and all the rest of health problems that you will learn through this paper.

In Part X you can find a little information on the most common psychiatric diagnoses for people suffering a quinolone reaction by their doctors.

PART I: INTRODUCTION

1. INTRODUCTION

Tens of thousands of people are damaged by quinolone (Cipro, Levaquin, Floxin, Noroxin, etc.) antibiotics each year, yet nearly all those damaged remain undiagnosed or misdiagnosed. Some are diagnosed as having fibromyalgia, multiple sclerosis, rheumatoid diseases, myositis, diverse heart problems or neuropathies of every kind. Thousands of people become severely crippled for years, or even permanently, after taking a quinolone antibiotic for minor infections.

Quinolone antibiotics are toxic from the very first milligram of ingestion. The effects of quinolone antibiotics are cumulative. Each person has a unique threshold of tolerance for the quinolones that once surpassed releases symptoms corresponding to various disorders, with long-lasting and potentially permanent damage. People are exposed to quinolones through taking them as a drug prescription or through food (chemically treated poultry and cattle).

Only a handful of doctors are aware of this devastating problem. The rest are uninformed, at least in technical matters, by the manufacturers. The drug manufacturers conceal the real toxic profile of the fluoroquinolone antibiotics. The manufacturers know they cause extensive damage, destroy lives and impair people for life, but they manipulate the trials, especially in not conducting any long-term follow up studies and under-reporting the adverse events. It is typical for manufacturers to state as "*very rare adverse events found in less than 1% of cases*", for adverse effects that have a real percentage above 70% for therapeutic doses.

Manufacturers have found a brilliantly disguised drug that in many cases wreaks havoc on its users some weeks or months after cessation of the drug therapy, or through food ingestion, making it almost impossible to trace back the symptoms to the real cause.

Recently (fall 2004), it has been made mandatory that the package inserts of the quinolone antibiotics must include a warning about "*rare*" adverse reactions that can cause irreversible neuropathic conditions. Up to now the possibility was simply systematically denied by the manufacturers because admitting it could harm their revenue. The Food and Drug Administration (FDA) also rejected any link between the thousands of individual reports on long-lasting and permanent damage caused by quinolones because their policy with respect to already marketed drugs is to delay as much as possible any warning that could alarm the people and show the inefficacy of the procedures and surveillance methods that they set to theoretically protect us.

Now, the overwhelming evidence has forced manufacturers and the FDA alike to admit irreversible damage. We had warned of it early in 2003, and many other groups of people and doctors are reporting such cases for at least the past 20 years. Now they try to avoid the sheer responsibility of indefinitely prolonging such a public health tragedy-- rating it as "*rare*". It is only a matter of time before they will have to admit that the extensive toxicity of quinolones is a class effect of this type of antibiotic, and that it affects everyone taking them, and that these drugs should be restricted to very special cases (life or death) of antimicrobial therapy.

Of special interest for athletes is the fact that quinolone and fluoroquinolone antibiotics cause many problems concerning the musculoskeletal system, most of which resemble other ailments that are acceptably known, diagnosed and treated (epicondylitis, shin splints, plantar fasciitis, overuse syndromes, trochanteric bursitis, all sorts of tendinitis, tenosynovitis and enthesitis, ulnar compression neuritis, iliotibial band syndrome, and many more). But the damage caused by quinolones does not respond to conventional treatments and leads to very disabling conditions, usually attributed to other causative factors (leg length discrepancy, worn shoes, lack of flexibility, muscle imbalance, over-pronation, supination, misalignments, wear, tear, etc...).

As a result, many of these problems are improperly diagnosed and remain elusive to all the treatments of choice devised for other pathologies. When conventional treatments (corticoids, steroids or anti-inflammatory medications) are used for disorders caused by quinolone antibiotics, they can cause great additional damage that can lead to tendon ruptures and permanent disability.

That is the reason why there is an imperative need for clearer and more honest information about this class of antibiotics called quinolones and fluoroquinolones. The present report is a summary of many real cases studied over the last several years that shows a closer picture of the real toxic nature of quinolone antibiotics.

The current version of the present report focuses mainly in SEVERE reactions experienced by previously healthy and young athletes. And, therefore, it is more focused on all areas relevant to physical and athletic performance. After studying dozens of cases in detail, the similarity between all of them is very striking. A few other hundred cases have been analysed in less detail to form the report.

As the report is large, some sections are repetitive, in order to facilitate and inform and they can be consulted quite separately. In the report we do not make any distinction between quinolone and fluoroquinolone antibiotics because both subfamilies share the same toxicity.

2. QUINOLONE FIRST FACTS

The fluoroquinolones are a class of synthetic antimicrobial agents which were modeled after nalidixic acid, a non-fluorinated quinolone antibiotic. Nalidixic acid was approved by the Food and Drug Administration (FDA) in 1963 for the treatment of urinary tract infections. It is rapidly absorbed after oral administration and is excreted into the urine in bactericidal concentrations. This compound has several limitations, which prevents its use in other types of infections. Specifically, nalidixic acid has a narrow spectrum of activity and microorganisms easily developed resistance to this drug.

During the 1980s, modifications of this drug were made. It had been discovered that a fluorine atom on the number 6 carbon and a piperazine ring at the number 7 carbon greatly enhance the spectrum of activity. These revisions to nalidixic acid's structure were responsible for improving the activity of these agents for Gram positive organisms and expanding the Gram negative spectrum to *Pseudomonas aeruginosa*, *Haemophilus influenzae*, and *Neisseria gonorrhoea*.

Much like other antibiotics, the 6-fluoroquinolones work to inhibit bacterial DNA synthesis and exhibit concentration-dependent killing of microorganisms. However, their mechanism of action is somewhat unique in that they inhibit the bacterial DNA gyrase, the enzyme responsible for DNA replication in such a way that irreparable breakages occur in the DNA strand.

Overall, with the exception of sparfloxacin, the fluoroquinolone antibiotics are rapidly absorbed after oral administration and reach their maximum concentrations in one to two hours. Food may decrease the rate, but not the extent of absorption.

All fluoroquinolones are eliminated by a combination of the kidney and the liver. Good renal function is important in the elimination of all of these antibiotics, even when only small amounts of unchanged drug are detectable in the urine.

Quinolones belong to the current arsenal of antibiotics developed to treat different infections and are useful to fight bacteria resistant to other antibiotics and for people allergic to more benign antimicrobials. They are also preferred for urinary tract infections because some of the antibiotics used in the past were so toxic to the kidneys or the auditory system for instance, originating thousands of dialysis patients and tens of thousands of deaf people.

3. WHAT CAN I EXPECT FROM TAKING A QUINOLONE ANTIBIOTIC

NOTE:

Everybody can have an allergic or hypersensitive reaction to any drug. Also, some people are good metabolizers (their livers can process the drugs easily) but others are poor metabolizers (their livers cannot break down drugs properly so they build up in the body up to toxic concentrations).

All the statistical and research data provided in this paper is based on experiences of people non allergic, not hypersensitive and considered as normal metabolizers.

Like many other, quinolones are highly toxic medications. The worst problem posed by quinolones is the severity and irreversibility of many of the lesions that they cause, some of which emerge well after finishing the treatment, when there is no possibility of stopping the ingestion of the drug.

In general, you should ask your doctor to prescribe another -less toxic- antibiotic, if there is an alternative, because all doctors with a knowledge on quinolones (including FDA officials) share the opinion that quinolones should be a second or third line antibiotics.

In any case, the toxicity does not show up with important symptoms if you take short courses and low doses. Used in low doses (250 to 500 mg of the equivalent to ciprofloxacin potency daily) for short courses (up to one week) these antimicrobials have a low toxic profile.

The whole problem with the quinolones comes from their very narrow safety profile, that is rarely respected.

Although is difficult to establish objectively the limits of what could be called "safe" or "unsafe", it is clear that the clinical practice for prescribing quinolones is generally well out of the safe margins. The inadequate and risky practices are:

- prescribing doses much larger than necessary
- prescribing courses much longer than necessary
- not adjusting doses for weight and build
- not testing the liver and renal functions prior and during long treatments

- not taking into account prior ingestions of quinolones and the cumulative effect
- not looking for adverse effects up to several months after completing the treatment
- dismissing or not identifying the first symptoms of the intoxications
- prescribing the quinolones to people under age
- not checking the interactions with other drugs and foods (caffeine, teophylline, grapefruit and many others)

Fluoroquinolone Utilization in the Emergency Departments of Academic Medical Centers. Prevalence of, and Risk Factors for, Inappropriate Use. Arch Intern Med. 2003;163:601-605.

We studied 100 consecutive ED patients who received an FQ and were subsequently discharged.

Appropriateness of the indication for use was judged according to existing institutional guidelines. A case-control study was conducted to identify the prevalence of, and risk factors for, inappropriate FQ use.

Results: Of 100 total patients, 81 received an FQ for an inappropriate indication. Of these cases, 43 (53%) were judged inappropriate because another agent was considered first line, 27 (33%) because there was no evidence of infection based on the documented evaluation, and 11 (14%) because of inability to assess the need for antimicrobial therapy. Although the prevalence of inappropriate use was similar across various clinical scenarios, there was a borderline significant association between the hospital in which the ED was located and inappropriate FQ use. Of the 19 patients who received an FQ for an appropriate indication, only 1 received both the correct dose and duration of therapy.

Conclusions: Inappropriate FQ use in EDs is extremely common.

The result is a very high incidence of adverse reactions, some of which impair people for life.

[The epidemic of sick people treated directly with quinolones](#)

Those safety principles stated above should only be overruled in critical cases, after assessing properly the risk-benefit ratio. However, less than 15% of all the quinolone prescriptions meet the safety criteria, hence the epidemic of intoxications that plagues people in all countries. In other words, being antibiotics with an extraordinary toxic potential, they are prescribed carelessly.

This epidemic is one of the least recognized for now and one of the easiest to avoid. The only thing at stake is the revenue of the manufacturers of these antibiotics, that not surprisingly are among the most expensive on the market. But that does not mean that they are expensive to produce and it is known that the development costs were recovered years ago.

This epidemic affects alike people that are very resistant to quinolones (whose bodies, specially their livers, metabolize properly the quinolones), and people that are hypersensitive to quinolones, poor metabolizers or intolerant to those medicines because of other reasons.

[The epidemic of sick people that take quinolones through food](#)

The "industry" (the manufacturers) produce quinolones massively for veterinary use. Some developing countries sell internationally quinolones for fish and cattle literally by the ton. Much of the poultry on the market in Asia, America and Europe has been raised fed with antibiotics (quinolones included) from the first day of their lives to the last, and direct to our plates.

Oddly enough, the medical associations and citizen groups are concerned only with the effectiveness of the antibiotics on the long run and not with the adverse health effects of antibiotics in our foods. They correctly advocate that new bacteria resistant to quinolones are housed by the birds, that can pass on to people and for which one day could be no treatment available. For that reason they postulate that quinolones should be banned for meat and fish production, to which the manufacturers of quinolones exert a strong opposition, putting into action their lobbyists at all political levels.

Although that worries are justified and seem appropriate, equally important is the fact that the content of quinolones in some food is far beyond reasonable amounts and cause sickness in people sensitive to them and in normal people by accumulation, not to mention to people that is recovering from a quinolone intoxication. Thus, there is another silent, low grade epidemic, the one caused by the intoxication got through ingestion of quinolones by food, which manifests as fibromyalgias, neurological problems of every kind, insomnia, psychical disorders, osteoarthritis, and others.

[4. WHO WILL BENEFIT FROM THIS REPORT](#)

You may find this report helpful if:

- You are looking for a connection between your recent physical problems and the drugs you have been taking lately.
- You are concerned about a prolonged course of fluoroquinolones (i.e. Cipro, Levaquin, Floxin, etc.) that you have been prescribed and are about to start.

- You may have taken quinolones in the past, and are planning to take a more prolonged course of these antibiotics, so you want to obtain more information and have a clearer picture.
- You are a medical practitioner and want to learn more about the patient's point of view regarding this dramatic health problem.

As you can learn through the paper, we have rated the reactions to quinolones as: MILD, INTERMEDIATE and SEVERE. Severe reactions are relatively unusual and really different to all the rest. This article deals especially with the implications of SEVERE reactions to fluoroquinolone antibiotics. Nevertheless, this report is not a reference for current long-term sufferers of quinolone toxicity because it does not add new information to the wealth of it already available.

HOW TO USE THIS ARTICLE IF YOU ARE A PERSON THAT HAS SUFFERED A REACTION TO A QUINOLONE

This article might be useful to help you to know where you are during the first stages when you are wondering what is happening to you, why, to whom ask for help. The article could contribute to overcome your disorientation. The article could save you erratic searches for answers and could contribute to get a general overview of this health problem. The article does not contain information that you cannot collect anywhere else after months of research.

This article must not be interpreted literally. It is not a manual for intoxicated by quinolones. You should not attempt to fit your case in any of the groups or scales provided herein, because they are average experiences. Many reactions have 80% or 90% of common symptoms, specially in severe cases, but in mild and intermediate intoxications there is a great variability about personal conditions, although always within the common trunk of the well known specificity of the reactions to quinolone antibiotics.

5. WHY HAS THIS REPORT BEEN WRITTEN

There is little or no medical information publicly available via the Internet for the general population that deals with the practical side of adverse reactions to quinolone antibiotics.

The only real information available to date comes the support groups sustained by sufferers. (We strongly recommend visiting the webpages:

www.fqresearch.org

www.drugvictims.org

www.medicationsense.com

Those sites belong to their owners and do not have any relationship with the authors of this report). In particular, www.fqresearch.org is a very comprehensive database on fluoroquinolone and quinolone antibiotics.

Nearly all the medical investigations in progress are not comprehensive. The researchers in charge have a sheer lack of knowledge about the real and true facts of this syndrome. Many investigations are very superficial, nearly anecdotal, and only look after a publishable paper, so that statistics of activity in the scientific group remain high in the annual report. There are myriad scope-limiting articles, all of which have contributed to extensive data, plus many, many instances of scientific evidence supporting the great damage that quinolones inflict upon people, but there is not a single comprehensive study about the adverse effects caused by quinolones.

No consistent clinical studies can be found that put the real figures of adverse effects where they really are. There is not a single study that shows the true extent of the damage caused by these antibiotics. There are multiple causes for this lack of proper investigation:

- The pressure exerted by drug manufacturers, the propaganda they spread in medical circles, and the counter-studies that they promote, most of which are unscientific creations of well paid doctors that show "evidence according to their personal experience" of maximum beneficial activity of the antibiotic and their "negligible" adverse effect profile. We can even see irresponsible and poorly educated doctors prescribing and recommending quinolones for children, when currently there is overwhelming evidence that quinolones cause cartilage and joint lesions of extreme severity in immature persons.
- The manipulation of the postmarketing adverse events done by the "industry" (laboratories), that make all that is in their hands to label the most appalling severe reactions to quinolones with the asertion that "univocal link of the event with the quinolone ingestion could not be proved" and thus dismissing most of the reports of serious reactions, and keeping the statistics of toxicity intentionally low. Manufacturers only consider the possibility of being before a quinolone reaction when a doctor states boldly that there was not any other concomitant agent causing the adverse event, or when the patient has been rechallenged by the quinolone and the reaction cannot be blamed on anything else.

- The delayed onset of symptoms is perhaps the most important fact that is universally ignored by doctors. Many researchers only monitor patients while they are on the medication and in some isolated cases "up to a month later". The vast majority of disorders appear months or up to a year and a half later and are therefore never linked with the real cause.
- The lack of knowledge and preparation of the doctors that prescribe them and the aspect that doctors nearly always dismiss their patient's complaints, and their refusal to admit any link between the severe and long lasting pathologies and their causal agent: the quinolones. The ignorance of doctors about the toxicity of quinolones is simply appalling, irrational and unjustifiable. Many doctors are handing out lifelong misery to their patients and destroying their lives forever.

This report will help the non-medical population know more about the true and real-life nature of quinolones. It can also be a call for the caring doctor to promote a more critical approach and perform unbiased professional research prior to prescribing quinolones.

We need to convince the medical class that:

- Until better antibiotics are developed, a defectively designed drug like a quinolone antibiotic should be restricted to emergency, complicated infections or life or death cases, but never used as a first line of treatment. Quinolones are not an antibiotic in the traditional sense, but a toxic chemotherapeutic agent, with very severe and long-lasting adverse effects.
- Thousands of affected people need help, and adequate research is urgently needed in order to determine the mechanisms by which these drugs cause their damage, and how to limit their effects.

It is a shame that patients and victims once again have to write reports like this, placing themselves years ahead of their doctors. In ten years time the essential information contained in this report will already be common knowledge for thousands of persons, and it will be "discovered" by the medical class and then become accepted knowledge. Too late for too many. Is this the medical class that we deserve?

Reminder:

Half of the quinolone antibiotics marketed in the last twenty years have been withdrawn from the market because of their great toxicity.

6. HOW HAS THIS REPORT BEEN WRITTEN

Nobody that has collaborated to create this article has had any previous reaction to any drug, food or allergen. We all were healthy people. We come from different backgrounds, races, social classes and we don't share any common physical aspect that makes us more prone to be injured by quinolone antibiotics. It only happens that we have managed to link our health problems to the exact agent that caused them. In nearly all cases, we noticed that the drug was damaging us during the treatment, but by then most of us had already taken the entire quantity of the prescription. Others reported to their doctors that the quinolone was causing pains but the doctors dismissed any link between the symptoms and the drug and asked them to continue on with the treatment; even though the patients themselves knew their bodies well as trained athletes and there was no doubt about what was happening. Some people started to feel bad after ending the treatment.

We have spent more than five years studying the floxing syndrome (quinolone toxicity syndrome or QTS), especially from the point of view of severe neuropathies, muscular and joint disorders-- with specific emphasis on the healthy, young, active and athletic population. Some doctors have contributed with their opinions or outcomes of small researchs that they have done in order to help us.

We have challenged ourselves with blind trials using placebos and active agents but always stayed away from potent drugs or supplements. We have kept detailed diaries for years with tens of thousands of entries recording ongoing symptoms and our attempts at regaining basic movement, fitness, and athleticism. We have probed and pushed ourselves through pains, endurance, and tests of many kinds, varying as few factors as possible in each trial, so that results could be of use. We have had more than a hundred MRIs (magnetic resonance image), dozens of CATs (computerized axial tomography), plain radiographs, three phase gammagraphies, dopplers, echographies, electromyographies, nerve conductivity tests, ultrasound tests, and hundreds of blood, urine, stool, and hair tests along with many other diagnostic tests as well as a few biopsies.

We have talked to hundreds of people suffering from this syndrome. We have used logical methodologies to draw many conclusions. Obviously, from observation, repetition and comparison alone, we cannot aim to discover the mechanism of damage, or the elusive clues for a healing protocol.

The main source of data used to write this paper comes from the experience of a cohort of people with the following profile:

| -TABLE 1- STATISTICAL PROFILE OF THE WELL STUDIED CASES RELATED TO THIS REPORT | |
|---|--------------------------------------|
| Number of persons | 42 |
| People with complete recording of data and battery of tests | 18 |
| People with partial recording of data and battery of tests | 24 |
| Sex | 78% male, 22% female |
| Age | 28 to 56; mean 39 years at the onset |
| People without any prior major medical problem: | 37 |
| People without any prior known allergy to medications: | 36 |
| People without any prior known immunological or rheumatic disorder: | 37 |
| People that suffered a mild reaction to quinolones | 6 |
| People that suffered a mild to intermediate reactions to quinolones | 11 |
| People that suffered a intermediate to severe reactions to quinolones | 16 |
| People that suffered a severe reaction to quinolones | 9 |
| Cases that were re-exposures (with unidentified prior reactions) | 6 |
| People had taken quinolones in the past with apparently no reactions | 8 |

But, in total, we, as many others, have demonstrated once more and beyond any doubt, the extensive and devastating effects of quinolone antibiotics and the unethical behaviour of the FDA and other western agencies that are dominated by the manufacturer's lobbies who routinely do not protect the people's health as they should, resulting in the increase of financial profit for the laboratories and pharmaceutical companies.

7. THE RULES OF THE THUMB ON ANTIBIOTICS

Most doctors only have slight notions about pharmacology and base their knowledge on brief and solid notions, that they tend to house as succinct and immovable medical principles. Those principles have been etched on them by the propaganda of the laboratories, be it through wonder tales of the salesforce or by biased and paid articles that praise the drugs in the medical publications. Therefore, reports and warnings about toxicity of certain drugs, raised by researchers are paid no heed for years until a massive epidemic of extremely severe or fatal events to thousands of people is unveiled.

With the quinolones antibiotics we are at this phase in which the toxicity has been identified, it has been demonstrated that it is a direct class effect (not very dependent on personal conditions), and that it is almost a guaranteed result of every quinolone treatment for some approved dosings and lengths of treatments, but mainstream doctors are still considering it a perfect antibiotic with a broad spectrum of activity and negligible adverse effects.

Many years ago all antibiotics were considered wonder medications with no important side effects but the risk of an allergic reaction. Millions of lives have been saved since their discovery. Later on the approach was broader and doctors started weighting all the pros and cons of prescribing antibiotics at the same time that medical research disclosed that there were some severe health risks linked to some class of antibiotics. For instance, today it is fully acknowledged that aminoglycosides have an extraordinarily high incidence of renal damage and irreversible deafness.

Quinolones have a very high potential to cause permanent neurological, vision and joint damages, and it is a matter of time that quinolones are widespreadly linked to high toxicity, and irreversible lesions. So, the updated rule of thumb when doctors prescribe antibiotics should be updated with the following contents:

| -TABLE 2- THE RULE OF THE THUMB OF THE USE OF ANTIBIOTICS | |
|--|--|
| Antimicrobial | Serious and FREQUENT reactions that are well known |
| <i>The list as it is now (in abbreviated form)...</i> | |
| Aminoglycosides | Nephrotoxicity, ototoxicity, mostly irreversible |
| Clindamycin (Cleocin) | Diarrhea or colitis, morbilliform skin eruption |
| Metronidazole | Neurologic toxicity |
| Tetracyclines | GI intolerance, candidal vaginitis |
| Etcétera.... | (this table is not a complete one) |
| <i>And with this adding that it should contain.....</i> | |
| Fluoroquinolones | Irreversible neurological damage. Permanent vision abnormalities Joint destruction |

PART II: TOXICITY OF QUINOLONE ANTIBIOTICS

8. QUINOLONE ANTIBIOTICS

The main quinolone and fluoroquinolone antibiotics and their full pharmaceutical names are as follows:

| | |
|----------------|---------------|
| Cipro | Ciprofloxacin |
| Levaquin..... | Levofloxacin |
| Penetrex | Enoxacin |
| Tequin..... | Gatifloxacin |
| Maxaquin | Lomefloxacin |
| Avelox | Moxifloxacin |
| Noroxin | Norfloxacin |
| Floxin | Ofloxacin |
| Zagam | Sparfloxacin |
| Factive..... | Gemifloxacin |

Many quinolones are routinely withdrawn from most markets. A recent example is trovafloxacin, that has been forbidden in Europe after "discovering" that it caused many liver failures requiring fulminant transplants and deaths, among other extremely severe damages, never associated before to the innocuous trovafloxacin. For health agencies to "discover" these kind of toxic profiles means that they are so overwhelmed by the evidence of many tragedies gathered through the years that they cannot longer please the requests of manufacturers to stay on the market and even increase the range of use and have to ban the drug.

Normally, manufacturers are very keen at manipulating the results of the final phases trials of drugs, and to conceal the risks for patients. The *industry* is also very proficient at pursuing and discrediting any independent report on adverse effects of their medications. As the manufacturers are the almost sole providers of information to the health agencies, the latter only act normally after years of having proofs that people were dying and being severely injured. You can learn more about the subject on many investigative and authoritative reports that have been published over the past years. Something more is treated briefly later in this paper.

By the way, trovafloxacin is still approved for use in the United States. Temafloxacin has been withdrawn recently due to very severe toxic effects.

Many quinolones are in the process of entering the market, both as generic forms and as new brands (all the manufacturers want to have a "me-too" compound that sells at high prices, so always find out to which class of antibiotics belong the one that you have been prescribed.

9. THE WAY QUINOLONES ARE INVENTED

After the development of the core quinolones, the ones on which all the rest are based, all pharmaceutical companies want to have one or several of them on their portfolio. For that purpose, they manipulate the original molecule, shifting positions of atoms and links around. The new chemical thus made has slightly different properties, many times impossible to discern, and they try to patent it and mass produce the stuff and sell it at high prices.

Some of these new quinolones have frequently extreme toxicity, that manufacturers make their best to conceal or to not unveil during the premarketing trials, and they finally enter the market, causing many deaths and fulminant damages until they are withdrawn as we have seen above.

Other quinolones are equally toxic as the parent ones, or have modified toxicities but still bear the delayed toxicity properties that are so convenient for not blaming the quinolones on the damages and injuries that they cause.

Up to now, all the quinolones marketed or in advanced stages of development have as a class effect the wide range toxicity reported in this paper: central and peripheral nervous systems, heart, liver, kidney and other systems, vision, cartilages and tendons and all the rest that you can consult hereafter.

10. TOXICITY OF QUINOLONE ANTIBIOTICS

Quinolones are very toxic antibiotics. They are not biological products but purely man-made chemical toxic compounds for killing bacteria, and ultimately, your body and its many structures and systems. High doses or prolonged courses cause a disproportionate percentage of adverse effects. Although most laboratories and manufacturers rate the number of adverse reactions as being very low, the real figures are much higher. These drugs are distinctive for one thing: for the vast majority of people, damage remains unnoticed for many weeks or months, which does not prompt the patient to stop the treatment, and then severe disorders develop with many clinical symptoms.

The mainstream medical class ignores this fact and is reluctant to learn that an antibiotic can inflict such severe, disabling and long-lasting damage. Consequently, nearly all victims of this drug toxicity are wrongly diagnosed as suffering from overuse injuries, neurological illnesses, immune reactions, osteoarthritis, cardiopathies, vision problems, etc.

For the purpose of this report we will call FLOXING SYNDROME the set of disorders caused by quinolone antibiotics. In medical terms it would be called QUINOLONE TOXICITY SYNDROME (QTS).

There is very little -if any- clinical knowledge about this syndrome, as it is not yet recognized as a major health problem, and no protocol for healing has been developed so far. There is not a single scientific study performed in order to better understand the true nature of the toxicity or to make a treatment available. Unfortunately, there are no specific tests or markers that can objectively diagnose the syndrome or the extent of its severity at any given moment. The vast array of symptoms that usually accompany a severe QTS (QUINOLONE TOXICITY SYNDROME) makes the task of establishing a reliable diagnostic procedure difficult and complicates the search for a cure.

Remember:

Quinolones are very toxic antibiotics. As it has happened with many other drugs before, the medical class still ignores it all.

This syndrome is so widespread, yet unrecognised, that it could constitute in and of itself, a specific kind of neuromuscular, systemic disorder that affects all body systems, and as a result deserves to be studied and treated separately as a branch of the drug-induced generalized disorders.

11. WHAT ELSE SHOULD BE INCLUDED IN THE PACKAGE INSERT?

The pharmaceutical package inserts for prescription quinolone antibiotics contain gross underestimations of severe adverse effects. These adverse events are presented as rare or very rare, when in fact they are very common or even unavoidable, that is to say, predictable, as it has been shown by some epidemiological studies.

In order to help you to get an idea of the real toxicity profile of quinolone antibiotics, take into account that had it not been for the manufacturer's manipulation and FDA consent, the package insert would read:

- *This drug is neurotoxic. The effects of this drug are cumulative, so ask your doctor to keep a record of the total amount ingested by you, so that currently supposed safe levels are not surpassed. The neuropathies associated with this drug (with sensory as well as motor and autonomic involvement) are often severe, lasting for many years or permanent.*
- *The therapeutic effects of this drug disappear with drug cessation, but the adverse reactions can manifest weeks, months or for up to two years later, so report to your doctor any abnormal bouts of neuropathies, central nervous system disorder like insomnia, nervousness, tendinitis, joint pains, muscle pains, twitching, fasciculations and/or body trembling, visual disturbances such as decreased visual acuity, dry eyes, blurred vision, double vision or other dry mucous symptoms (mouth, nose, skin, ears, etc...) as well as all the rest of symptoms listed in the package. In many cases the resolution of symptoms takes several years.*
- *This drug will deteriorate the cartilage all over the body as it kills the chondrocytes, the root cells of cartilage. The damage depends on the previous state of you cartilage, plus the dose and length of quinolone treatment. Do not take this drug if you suffer from early osteoarthritis, if you frequently play sports or perform strenuous tasks or exercises. Usually, the damage inflicted is irreversible.*
- *This drug is not recommended for those who have been diagnosed with autoimmune disorders, or if there is a suspicion about one being present. It can cause conditions similar to, as well as worsen or release, autoimmune disorders like multiple sclerosis, lupus erithematosus, rheumatoid arthritis, small vessel vasculitis, dermatomyositis, polymyositis and others.*
- *Quinolones can cause fatal arrhythmias and other heart lesions. Do not take them if you suffer from any heart condition or a history of palpitations or irregular heartbeats.*

- Elderly people, diabetics, patients with impaired renal function, persons under 18 (whose bones and cartilage are still growing) and people taking corticoids are at great risk of suffering very disabling reactions.

All of these statements will be acknowledged by the medical community in the years to come, only too late for thousands of people whose lives will have already been meaninglessly ruined.

Take notice:

Quinolones cause permanent lesions, especially degeneration of cartilages in knees, hips, spine, and shoulders, plus irreversible damage in the eye, fatal arrhythmias and irreversible neurological disorders.

Keep in mind that half of the quinolone antibiotics marketed in the last twenty years have been withdrawn from the market because of their great toxicity. The quinolones currently available are just slight variations (shifting the position of one atom or molecule) of the openly toxic quinolones, and are still very toxic. The magic of the new position of the atom is that the toxicity is more concealed, cumulative, internal, and mimics other serious illnesses.

12. REAL RATES OF ADVERSE REACTIONS

There are enough published reports and Rx lists about these drugs. You can find them on the Internet. The list of adverse effects for each quinolone drug is extensive, and many of the adverse reactions will manifest in normal people with long treatments or high doses, or just with one pill in extreme cases of intolerance.

Remember that the "rare" frequency of adverse reactions stated in the pharmaceutical package inserts is usually grossly underrated. The statistics provided by the manufacturers are a gross manipulation of biased clinical trials, and are totally unreliable. For a better assessment of your chances of getting seriously ill, consider the table 3 instead. We do not understand either why the package inserts do not discern among probabilities of having adverse reactions for different lengths of treatments or why they do not adjust the doses for body weight, age, or liver and renal impairments.

Let us suppose that you are a healthy, young person, you are not taking any other medications and that you are the perfect patient- not allergic to anything and able to metabolise most commonly marketed drugs without experiencing adverse effects; then your chances of developing clinical symptoms of serious disorders caused by a quinolone antibiotic are:

| -TABLE 3- Adverse effects occurrence for quinolone antibiotics (using as reference ciprofloxacin potency) (people of up to 160 lb of body weight) | | | | |
|---|-------------------------------|--------------|------|--|
| THERAPEUTIC REGIME /DOSAGE | PERCENTAGE OF ADVERSE EFFECTS | | | DURATION OF THE ADVERSE EFFECTS |
| | SEVERE | INTERMEDIATE | MILD | |
| up to one week of up to 1,000 mg daily | 9% | 22% | 29% | several weeks to months |
| 6 weeks of 1,000 mg daily | 62% | 91% | 100% | months to years |
| more than 6 weeks on a 1,000 mg/day basis | 86% | 100% | 100% | mean duration of severe limitations and pains for 2.5 years, but can be 6 years more - and in some cases the damage and destruction is permanent or ends in death. |
| 1,500 mg/day for a week or more | 100% | 100% | 100% | Many years or permanent |

We have talked with nearly 50 people who thought that their quinolone treatment had been successful and without any adverse effects who reported having had their first experience of severe bouts of tendinitis or neurological problems a few weeks or months after the quinolone treatment and therefore had not linked them with the drug. The same can be said about neurological disorders. Taking into consideration all the facts, nearly all of them now believe that the cipro or levaquin they took is the cause of their insomnia, peripheral neuropathies and musculoskeletal problems. There are also many medical papers confirming that many of these damages become symptomatic months after finishing the treatment.

The recent experience with the U.S. postal workers (some thousand treated with up to 60 days of ciprofloxacin) presents figures very similar to those in table 3. It is the first time in history that a large group of people is treated with quinolones for an extended period of time. For instance, in a medical survey study on that population, conducted by the Center for Disease Control, the federal agency based in Georgia, only one month after the therapy, 70% of patients had one or more adverse effects after the first half of the treatment (30 days); 25% of patients had joint problems after the 30 day mark; 23% of people experienced fainting, dizziness, or seizures in that month. These figures have been a sort of a shock for the doctors in charge of the survey.

The report on the postal workers has not included the rates of adverse events after 60 days of treatment, but surely they would have neared 100%, even more if the workers had been re-questioned some months after cessation of the therapy. So, where is

the supposedly “rare incidence of less than 1%” that cipro boasts in its package insert? And why hasn't the FDA drawn any conclusions from this experience 2 years after the survey was done? There is a strong opposition from the drug manufacturers and the FDA to study this field experience in detail; once again to avoid responsibilities and/or liabilities with respect to the workers. With this irresponsible attitude, many more thousands will keep enlarging the group of the quinolone-damaged persons.

Observation:

For long-term or high dose treatments, the adverse reaction rate reaches 100% of patients. Many people are unaware that their illness is a manifestation of quinolone toxicity.

There are persons that develop a very acute reaction after one single pill that normally matures into an intermediate reaction (see later) that lasts for 1 year on average. This aspect needs to be studied by scientific groups because perhaps it would give some clues in the search for an understanding of this disorder.

13. WHAT ABOUT THOSE PEOPLE THAT DO NOT SUFFER ADVERSE REACTIONS?

Many of us that have been seriously and/or irreversibly damaged by quinolones had successfully taken quinolones in the past. People have different susceptibilities to drugs, and there are many persons that can take diverse courses of quinolones with no adverse effects (when they are questioned properly they discover that they were having low grade symptoms). Many individuals can take quinolones without having very noticeable side effects, for instance:

- long treatments of 250 mg of ciprofloxacin daily
- 2 treatments per year of 7 days of 2x500 mg of ciprofloxacin daily, for several years

A lot of people do not exceed those limits, and therefore they feel the drug is doing great for them, although it is building-up a cumulative process that in the future could cause long term health problems.

Many floxies that thought that the quinolones worked very well with no side effects for their sinusitis, got seriously damaged when they were prescribed prolonged courses (6 weeks) of ciprofloxacin, or when the doctors prescribed a higher daily dose.

PART III: SYMPTOMS OF BEING INTOXICATED BY QUINOLONES

14. ARE YOU POISONED BY A QUINOLONE ANTIBIOTIC?

If you have taken a course of any quinolone or fluoroquinolone antibiotic (Cipro, Levaquin, Floxin, etc...) you have been chemically poisoned. Depending on individual conditions, and the dosage and length of the treatment, the intoxication will range from very mild and asymptomatic to very severe and disabling.

In a minority of cases, the patient notices the reaction immediately. In a vast number of cases, most symptoms, or at least the most severe ones, emerge during the last stages of the treatment, or weeks or months after the completion of the quinolone treatment.

Sedentary people tend to notice less adverse reactions because they do not use their body to full active capacity. Taking into account that at least one third of QTS presentations are predominately tendon-related or musculoskeletal, damage to their tendons, cartilages and muscles remains unnoticed.

Many people can take a 7-day course of quinolone antibiotics without perceiving any adverse effects. Their cartilage, tendons, nerves and small veins and arteries have been directly damaged but not enough to make them symptomatic. That is the case of many sedentary people who deeply damage their joints as a result of repeated but short courses of quinolones. But the fact remains unknown to them since they are asymptomatic, and they do not use their joints beyond the pain threshold. Later in life, it manifests as early osteoarthritis, collagenous deterioration, or nervous system failures. In any case, this paper is not intended for these people.

Many of us were healthy young athletes in perfect health with rock solid knees and hips prior to taking quinolones, but now have become crippled persons, with our cartilages half destroyed, our eyes barely functional, our bodies aching since several years ago and our whole lives stolen from us by a medical class that now turns its back on us.

For those that have developed symptoms like the ones described later, first of all, they have to check if they have ingested any quinolone antibiotics during the last three or four years. The damage caused by the quinolone antibiotics becomes evident at a point in time that ranges between the moment of the treatment itself from up to eighteen months later. If your symptoms fit with any of the categories listed later in this article, and you have taken fluoroquinolones in the past, then a quinolone induced intoxication might well be the reason for all of your recent physical problems. This report could help assist you in reaching a diagnosis.

15. SOME MEDICAL TERMS AND INFORMATION

This paper intentionally has a non-medical quality. However, it is necessary that you become familiar with a few technical facts regarding the floxing syndrome. Some are explained throughout the report, when they are needed. A brief introduction to the general aspects of an adverse drug reaction is included here.

The terms drug allergy, drug reaction and some euphemisms (hypersensitivity, intolerance) are often used interchangeably. If we take into account the immune response of the patient, a drug allergy can be restricted to the reaction in which special antibodies of the IgE type are massively released. This report does not cover allergic reactions.

Like many other drugs, quinolones can cause an immunologic type I reaction, plus many non-immunologic primary pharmacological side effects (insomnia, restlessness, caffeine intolerance) and secondary pharmacological side effects (thrush, leaky gut). They can also interact negatively with many drugs. But their distinctive actions are probably due to their direct toxicity and the subsequent immunologic reaction.

In most cases, there are not any markers that can confirm a diagnosis, so all serum (blood) parameters can be normal and one can still be suffering from a very severe and incapacitating reaction. Only a very specialized and often inaccessible (in most healthcare systems) tissue biopsy can confirm the problem and even then the probable denervation and cell degeneration shown will be classified according to standard methods and fit partially into already known diseases. Therefore, without a biopsy, most

diagnostics are established upon clinical symptoms. In principle, the fluoroquinolone syndrome can be classified as a TYPE III immunological reaction, with an added non-immunological TOXICITY.

Drug reactions can be classified as follows:

| -TABLE 4- TYPES OF DRUG REACTIONS | | | |
|---------------------------------------|---|-------------|----------------------|
| TYPE | Specific | Key feature | Caused by quinolones |
| IMMUNOLOGIC | | | |
| Type I reaction | IgE mediated | Allergy | Yes, rare |
| Type II reaction | Cytotoxic | | Yes, common |
| Type III reaction | Immune complex | | Yes, typical |
| Type IV reaction | Cell mediated, delayed | | Yes, frequent |
| Specific T-cell activation | | | ? |
| Other | Chemical | Unknown | Yes, common |
| NON-IMMUNOLOGIC | | | |
| Primary pharmacological side effect | Direct problem associated with the drug | | Yes |
| Secondary pharmacological side effect | Opportunistic health problem | | Yes |
| Drug toxicity | Toxicity to organs and systems | | Yes |
| Interactions between drugs | Like with all drugs | | Yes |

Some classifications have been established in order to help discern among drug IMMUNE reactions:

| -TABLE 4-cont'd- TYPES OF IMMUNE REACTIONS | | | |
|--|---|---|--|
| Immune reaction | Action | Clinical symptoms | Timing of reactions |
| Type I reaction | Allergy (not covered by this report) | | |
| Type II reaction | Specific IgG or IgM antibodies directed to some cells | Blood abnormalities (neutropenia, anemia) | Variable |
| Type III reaction | Deposition of drug antibody complexes in several tissues, with complement activation and inflammation | Arthralgias, vasculitis, rash, serum sickness | 1 to 3 weeks after drug exposure or even many months later |
| Type IV reaction | Cytokine and inflammatory mediator release | Rash, contact dermatitis | 2 to 7 days |

One thing is clear: re-exposure to quinolones, after having been floxed previously, poses very high health risks for the patient. Persons that become floxed twice have the worst prognosis (expected outcome). Many people with moderate reactions to quinolones are later re-exposed to another round of the same antibiotics by their doctors that dismiss their complaints about pains and disorders associated to the antibiotic. The outcome is frequently a severe reaction that lasts 3 to 6 years and ends up with permanent lesions.

16. WHAT KIND OF DAMAGE DO QUINOLONE ANTIBIOTICS CAUSE?

This class of antibiotics has very characteristic ways of causing lesions:

- they damage the central and peripheral nervous systems
- they damage small veins and arteries (vascular disorder of the vasa vasorum and vasa nervorum)
- they impair the rebuilding and repairing capacity of tissues, specially connective-collagenous
- they chemically destroy important structures, like cartilage

There are many other mechanisms of quinolone assault on the human body (for instance, liver, kidney, pancreas and heart reactions, all of which can be serious or even fatal), but they are not the focus of the present report.

Important fact:
Pain and disability caused by quinolones is very long lasting and affects many parts of the body. In favorable cases recovery takes several months to years. In severe reactions pain and lesions can last for life.

17. HINTS AND CLUES THAT MIGHT SAVE YOUR LIFE

Perhaps you have taken quinolones in the past and you think that they worked well and that you did not react negatively to them. Check the following subtle symptoms and the normal interpretations that people make of them.

- You had a strange bout of tendinitis, for instance in the outer tip of the hip, normally diagnosed as trochanteric bursitis caused by tight belts or resting on you side. The same applies to other areas of the body, like the elbow (epicondylitis) diagnosed as an overuse of your tennis racquet or gardening practices, but you remember that you had never had it before.
- It takes you longer to recover after exercise. It is not alarming and you have not paid much attention to it.
- You sleep worse than before; it seems normal as you have a lot of pressure at work.
- From time to time you have some small throbbing pains in different parts of the body. They last only for a few seconds, so there is nothing to worry about it.
- It is strange- but you have occasional twitching in an eyelid, or any other part of the body. It is not painful.
- Some nights you feel some mild itching migrating along your body. One brief itching here and another there. It is more intense in the scrotum or groin. Instead of identifying it as a peripheral neuropathy you conclude that it must be your clothes or the new brand of soap that is more irritating.
- You feel some stiffness, especially in one or both legs, but it is normal because you are getting older.
- You do not tolerate coffee as well as before.
- Your memory is not as good as it used to be. The cause may be too many things to think about and too much stress. And you are no longer a young person.
- There is an urge to urinate when the bladder is partially full. Most urologists think that it is due to a dysfunction associated with a benign enlarged prostate but in reality it is a neurological deficit caused by the prescriptions of quinolones that they gave you.
- Some times, you have some very frightful dreams when getting asleep that scare you. How strange you think. They are toxic pannick attacks that reflect toxic damage of your brain.

If you have experienced some of these symptoms since you took your first quinolone, perhaps you have reached your first threshold of tolerance, that -once surpassed- can result in the destruction of your life soon thereafter if you take more quinolones.

18. WHAT ARE THE MAIN SYMPTOMS OF BEING POISONED BY A QUINOLONE?

Getting floxed is just getting intoxicated, or poisoned. The toxic agent (the quinolone compound) enters the blood stream and spreads throughout the body. The defenders of the quinolones are even proud of the big penetrative power of the drug, that reaches delicate organs like the brain that are very well shielded against most chemical compounds. Therefore, it is not surprising that symptoms of the toxicity arise over all body areas and systems.

For a complete list of symptoms - see later in the report. A strong reaction generates some 30 to 50 symptoms. In some cases adverse reactions appear right after the ingestion of the antibiotic. In intermediate and severe reactions you may start with a few symptoms and as time passes new and debilitating symptoms arise, especially around the second, sixth and ninth months mark post-floxing . And in many cases of young, very healthy and active people, the worst lesions emerge progressively up to eighteen months or more after the cessation of the drug (we have deducted it beyond any doubt from various crystal-clear cases plus several unwilling re-exposures with quinolones). There are many medical articles as well, that state that a lot of the drug induced symptoms start some weeks to months after completing the treatment.

Here we include the most easily recognizable and common symptoms in three groups. Please take into account that the heading of the three groups is only for orientation purposes. Some of the disorders are cytotoxic or vascular, for instance, and the headings do reflect that fact. Some lesions have a multiple root like eye damage that can be muscular, neurological, vascular and toxic but are included just in one group for the sake of simplification.

Joints and muscles:

- Arthralgias (pain in joints) specially the Achilles tendons, ankles, knees, hips, elbows, shoulders, wrists, neck. Pain of different kinds, very frequently migrating around a joint and then moving to other joints over time. Pains are bearable sometimes but they often are very debilitating, requiring almost absolute rest for months because patients cannot walk at all or more than a few paces or stand up for long. Even if the patient is functional, pains have a neurological root and can be very intense and interfere with normal activities and prevent sleep. These arthralgias evolve to osteoarthritis in many cases with cartilage erosions. The arthralgias start as early as during the antibiotic treatment. In other cases arthralgias show mildly at the beginning and their intensity increases to its maximum intensity up to a year and a half later. For athletes with this type of delayed reaction, a medium level of pain can be constant but some six hours after exercise the symptoms may be present as acute pains that can be excruciating if the limit of tolerance is reached. This limit consists of the maximum exercise that a given body can tolerate before its impaired repairing capacity is overwhelmed by the physical demands. For the average floxed athlete, this limit is much lower than it was before the quinolone intoxication.
- Pains in different areas of the body not considered main joints. Pains tend to be generalized and migrating. Can be mild or very intense. Common areas affected are the back, neck, head (jaw, skull zones), chest (breastbone), groin, testes, plantar fascia (sole of feet) and others. They can be very debilitating. Pains in many muscles over the body (myalgias), that cause a lot of stiffness and soreness. These pains are of every kind, like diffuse, acute, throbbing, pulsating, vibrating, burning, shooting, stabbing, dull, deep, tremors, and many times they increase at night. A floxie can feel pains walking, changing positions when sitting, being unable to cross legs or make some body torsions. In severe cases the pain lasts for five to six years on average.
- Acute tendinitis over different parts of the body very similar to normal types of tendinitis but different in its persistence and unresponsiveness to conventional treatments. This type of tendinitis is very acute at times, requiring immobilization, and is nearly always triggered by a level of use that was normal in the pre-floxed state, or normal daily use. The tendinitis does not respond to anti-inflammatory medication, which in fact, can make the symptoms worse. Sometimes the tendinitis migrates within a joint and from one joint to others. In the first stages of the floxing, the tendinitis is predominantly enthesitis, which is inflammation of the insertions of muscles and tendons into the joints. In many cases they end up in partially or fully ruptured tendons (achilles, shoulder rotators, wrists flexors). It is a class effect of all quinolones, in other words, all these antibiotics are very toxic for all the tendons in the body, for everybody. For every one- the quinolones cause small and multiple lesions in the tendons, that eventually rupture in those people unlucky enough having weak tendons, having taken corticoids, having pre-existing vascular problems (pre-diabetics) or being magnesium deficient. Long- term floxies, usually affected by a severe reaction still have tendinitis in critical areas of the body 4 or 6 years post-floxing. Very typical long term tendinitis are: plantar fascia, achilles tendon, posterior tibialis complex, insertions of knee's tendons, both ends of the ileotibial band, iliopsoas area, shoulder rotators, elbow epicondyle, forearm and wrists.
- Arthritis-like symptoms. Many symptoms resemble those of rheumatoid arthritis and other autoimmune diseases, but are always sero-negative and with a different pattern of clinical symptoms.
- Osteoarthritis-like symptoms. Joints usually start to make a lot of noise. After the intoxication, and with time, healthy cartilage becomes softened and erosion takes place, and the illness presents itself as a true clinical osteoarthritis. Knee cartilages are specially targeted by quinolones, with a very high incidence of torn menisci (inside the knee). There are many cases of complete destruction of previously healthy joints and the patient has to be submitted to very invasive surgical procedures and or total joint replacement. The most damaged cartilages are the most weight bearing ones: knees, hips and low spine. Cartilages of people that have taken several short-term quinolone treatments, as well as cartilages of those that have taken prolonged courses or high doses, have a very decreased bearing capacity.
- Permanent stiffness that exhibits a clear loss in range of movements, especially with legs and arms, but that can affect the whole body. The most affected joints are the hips (adduction, abduction, flexion and extension), knees (flexion, adduction), shoulders (extension). Increased stiffness after exercise. It takes longer to recover from exercise, and there is a clear loss of flexibility. Soreness in many muscles, especially legs and shoulders, with there also being a predilection for the neck. Weird sensations in the muscles and joints. Clear feeling that something is going very wrong.
- Shallow breathing that causes a deficit of oxygenation that complicates insomnia, recovery and other reactions and metabolisms in the body. During the acute phase the floxie can have a sense of not grasping enough air and subsequent sense of dying.
- Very slow recovery from impacts and blows. Whenever the affected person is hit in athletic or daily activities, the flesh takes much longer to recover from the pain, along with increased haemorrhaging and inflammation. Dark veins, haemorrhage-like patches under the skin.
- The skin (and other collagenous tissues) loses nearly all capacity of recovery. A cut on the skin near an affected joint leaves a pink scar for many months afterward whereas it would have become unnoticed in a pre-floxing state.
- Cold feet and hands. The presentation resembles Raynaud's syndrome. In many severe cases several phalanges of fingers

turn numb or become close to frozen with cold conditions that did not cause any trouble before the floxing. Loss of sensitivity in hands and feet. Increase in the shape or depth of vertical ridges in fingernails. Pains in the nails of the big toes that feel as if they were about to fall apart.

- Chest pain. Heartburn.
- Weight loss, probably due to muscle destruction and atrophy and alterations in intestinal function.

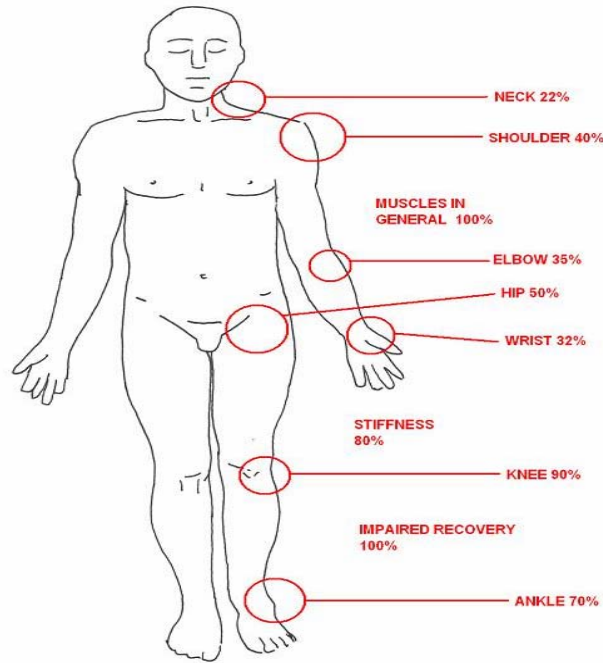


fig.1. -frequency of musculoskeletal disorders in severe reactions-

Central and peripheral nervous system and systemic:

- Brain fog, depression, depersonalization, short-term memory loss, and lethargy. Slurred speech. Inability to speak fluently. Forgetting words, getting stuck in the middle of a sentence. Some are caused by the insomnia but it is mainly a neurological lesion of the brain. Headaches, especially unilateral, or affecting one side only. Foggy mind, drowsiness, lethargy, loss of drive and power. Need to sleep. Tiredness and intense fatigue.
- Twitching, numbness, sensory disturbances, trembling, throbbing, pins and needles sensations, and pulsating pains in muscles and joints are the hallmark of this disease; especially in the lower legs (ankles, Achilles, calves, thighs and knees) arms and hands, but can manifest all over the body. Fasciculations (visible crawling under the skin) of muscles, due to denervation, a very serious neurological symptom. Twitching is manifested earlier in eyelids and the triangle on the back of the hand placed between the thumb and index finger before it can affect the whole body.
- Insomnia, very acute and difficult to deal with. Restlessness, great loss of sleep quality. Intolerance (great nervousness or increasing symptoms) to concentrated coffee (espresso) and tea. Intolerance to coffee can be present for more than 7 years. Insomnia can last more than 3 years during which is difficult to get more than a few hours of disrupted and bad quality sleep. Anguish, depression, pre-seizure state. During some part of the floxing most people experience anxiety and panic attacks (awakening amidst strange nightmares with fear and a feeling of dying), especially at night or when falling asleep.
- Vision problems. Diplopia (double vision) and other focusing problems. Large amount of floaters (dark worm, cobweb, string or spot like) that seem to float in the vitreous area of the eyes. Also ziggies (brilliant minute lights that move in a zig-zag or wavy, wandering manner in your field of vision). Sparks (flashing lights). Halos and curtains of watery sight in the upper part of the field of vision that move sideways along with your eye. Waves-like in the outer margins of the sight. Acute photophobia or intolerance to strong sunlight or artificial light. Complete or partial loss of vision (transitory, but lasting up to 6 minutes as absolute blindness seeing only solid white). In extreme cases, complete irreversible blindness has been documented in medical papers. Eye pain, ocular pressure, blurred vision. Loss of vitreous acuity. Cataracts, macular degeneration. Quinolones cause degeneration of the retina, especially the outer margins. In many cases, some very worrisome implications such as dry eye syndrome are also experienced. Dry eye can render 0 mm of tear absorption in the Schirmer's test. Vision damage reaches its peak about two to six months post-floxing and lasts for years or becomes a permanent lesion,

being a marker of the likelihood of recovery (i.e. the drier the eye and longer lasting, the lesser are the chances of overall recovery). Vision damages caused by quinolones have a high ratio of irreversibility. Severe reactions have nearly always associated some degree of damage on the vision, that is invariably assessed by the patients as very disabling. We have seen so many, really a great many, cases of irreversible damage of vision, or lesions not cured by the 5th year mark, and the distress inflicted on the sufferers, that this alone would be enough cause to withdraw all the quinolones from the market for primary care treatments.

- Diminished erectile function (semi-impotence). Difficulty to reach hard erections. Decreased sex drive (libido) both for men and women. Can last more than three years in severe reactions for young people that were very healthy and active sexually pre-floxing.
- Digestive problems. The quinolones damage the entire nervous network governing the intestines. Alteration of intestinal movements. Intolerance to foods and many compounds. Bad reactions from defectively digested foods. Inability to absorb some nutrients, especially minerals. Weight loss. Destruction all of the flora and proliferation of bad fungi like candida.
- Violent rectal spasms that may cause fainting. Spasmodic pains of every sort and intensity in every part of the body: skull, lower head, neck, jaw, shoulders, arms, back, hips, legs, ankles, fingers and toes.
- Trembling of a limb after sustaining tension with the muscular groups of that limb. For instance, trembling of the leg after toe-raising for a while, or an inability to write steadily after holding a heavy load with that hand.
- Tinnitus, or ringing in the ears. Ear pressure, usually in waves of pressure. Hypersensitivity to normal sound. Headaches, head pressure, mainly asymmetric. Hearing loss that can be permanent.
- Heart palpitations and strange pounding and throbbing. Skipped heart beats. Alterations of heartbeat. Irregular heartbeats are usually more common after eating. The heart palpitations and arrhythmias are some times life threatening. A serious heart condition called prolongation of the QT-interval is a class effect of all the quinolones, showing once more that they are very defective drugs. Some times floxed persons require the implantation of pacemakers. Many thousands of people die from heart attacks that are not of an infarction kind but cardiopathical, caused by defective nerve signals. Nearly all of them are caused by toxic compounds, like environmental hazards or medications, among them the quinolones (none of them are attributed to the real cause).

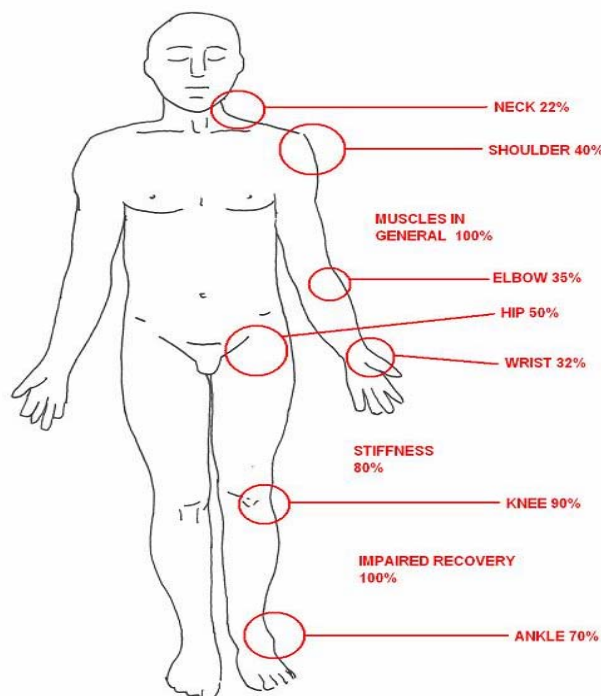


fig.2. -frequency of systemic disorders in intermediate and severe reactions-

- Neuropathies in limbs, with a lot of pain with muscle wasting and nerve involvement. In many cases they resemble muscular injuries. For instance, a femoral (upper leg) nerve neuropathy can be considered a pull in the hamstring; a peroneal nerve neuropathy can be disguised as an ankle strain, or an overuse syndrome and so on. These neuropathies have a rapid onset and grow in intensity for many months. In many cases it takes several years to get a remission of these neuropathies.
- Alterations of liver, kidney and pancreas enzymes and parameters. While taking quinolones the cholesterol and tryglicerides skyrocket up to three times their normal values, to return to normal range in a few weeks. Quinolones also provoke hypo- and hyperglycemias as a class effect. The quinolones accelerate the progression towards full diabetes of those individuals with an unrecognized pre-condition.

Autoimmune like responses:

The main symptoms of a quinolone poisoning resemble those of some autoimmune disorders because in acute intoxications they cause a type of small vessel vasculitis with neurological dysfunction:

- Dry eye, dry mouth, dry sinuses, dry ear and a shift towards dry skin. Dry eye can be measured with moisturizing stripes rendering null values in severe reactions. Sticky, gritty eyes. Dry eye can have serious consequences if not treated. Dry mouth, especially at night or when taking any vasodilator. Dry sinuses cause many infections that are also opportunistic due to the compromised immune system of the severely floxed persons. Dry ear turns the protective earwax into a sort of useless sand dust.
- Problems with foods and drinks. Your intestines are also altered and their permeability and ability to process foods is impaired. Abnormal intestinal function, food intolerances, chemical disturbances, cycling of symptoms and general malaise. Increased sensitivity to chemicals, especially to quinolone-tainted foods (poultry, beef). Sensitivity to perfumes, health care products and chemicals. Taste and smell perversions. Lack of sense of smell.
- Cycling or relapsing of symptoms. After the acute phase, nearly all recoveries experience cycles of improvement and relapses.
- Many symptoms that resemble fibromyalgia, multiple sclerosis, lupus erythematosus, rheumatoid arthritis, reactive arthritis, vasculitis, AIDS and other diseases.
- Skin rashes, especially in distal areas (hands, ankles). Itching, all over the body, with little intensity, plus more intense in some specific areas (hips, for instance) when taking a hot shower, plus itching in the groin and scrotum at night when hot. Reddish or red-blue upper eyelids. Increase in vertical ridges in nails of toes and fingers.

19. TYPICAL ADVERSE REACTION LIST OF A QUINOLONE ANTIBIOTIC

The following is the list of typical reactions observed during quinolone therapy. The list is an official one. It is comprehensive, but does not mention the severity of the reactions, and also, the percentage of people affected has been manipulated to appear as very low, when indeed it is much higher. Underlined are the reactions experienced by people related with this report.

Pregnancy Risk Factor and Implications: Category C, is excreted in human milk, potential for serious adverse reactions in nursing infants.

Contraindications: Do not use if you have a known allergy to ciprofloxacin or to any member of the quinolone class of antimicrobial agents.

Warnings/Precautions: The safety of this drug in pediatric patients, people less than 18 years old, pregnant and lactating women has not been established. This drug may cause cartilage erosion of weight-bearing joints. This drug may also cause convulsion, intracranial pressure, toxic psychosis, and it may cause central nervous system events. Use with caution in patients with CNS disorders or in patients with risk factors such as certain drug therapies and renal dysfunction that may predispose them to seizure or lower their seizure threshold. Serious and fatal reactions have been reported in patients receiving concurrent administration of ciprofloxacin and theophylline. Serious and occasionally fatal hypersensitivity reactions have been reported in patients receiving quinolone therapy. Severe hypersensitivity reactions characterized by rash, fever, eosinophilia, jaundice, and hepatic necrosis with fatal outcome have also been rarely reported in patients receiving ciprofloxacin along with other drugs. Pseudomembranous colitis has been reported with nearly all antibacterial agents including ciprofloxacin, and may range in severity from mild to life-threatening. Treatment with antibacterial agents alters the normal flora of the colon. Achilles and other tendon ruptures that required surgical repair or resulted in prolonged disability have been reported with ciprofloxacin and other quinolones. Avoid excessive sunlight as moderate to severe phototoxicity manifested as an exaggerated sunburn reaction has been observed in some patients while on the quinolone class of drugs.

Adverse Reactions: At least 5% experienced: Nausea

Adverse Reactions: Less than 5% experienced: Diarrhea, vomiting, abdominal pain/discomfort, headache, restlessness, rash, palpitation, atrial flutter, ventricular ectopy, syncope, hypertension, angina pectoris, myocardial infarction, cardiopulmonary arrest, cerebral thrombosis, dizziness, lightheadedness, insomnia, nightmares, hallucinations, manic reaction, irritability, tremor, ataxia, convulsive seizures, lethargy, drowsiness, weakness, malaise, anorexia, phobia, depersonalization, depression, paresthesia, painful oral mucous, oral candidiasis, dysphagia, intestinal perforation, gastrointestinal bleeding, cholestatic jaundice, arthralgia or back pain, joint stiffness, achiness, neck or chest pain, flare up of gout, interstitial nephritis, nephritis, renal failure, polyuria, urinary retention, urethral bleeding, vaginitis, acidosis, dyspnea, epistaxis, laryngeal or pulmonary edema, hiccough, memophysis, bronchospase, pumonary embolism, pruritus, urticaria, photosensitivity, flushing, fever, chills, angioedema, edema of the face, neck, lips, conjunctivae or hands, cutaneous candidiasis, hyperpigmentation, erythera nodosum, blurred vision, disturbed vision, decreased visual acuity, diplopia, eye pain, tinnitus, hearing loss, bad taste, vaginitis, headache, vaginal pruritus, abdominal discomfort, lymphadenopathy, foot pain, dizziness, breast pain, nausea, diarrhea, central nervous system disturbance, abnormalities of liver associated enzymes, eosinophila, restlessness, rash, cardiovascular collapse, cardiopulmonary arrest, myocardial infarction, arrhythmia, tachycardia, palpitation, cerebral thrombosis, syncope, cardiac murmur, hypertension, hypotension, angina pectoris, convulsive seizures, paranoia, toxic psychosis, depression, dysphasia, phobia, depersonalization, manic reaction, unresponsiveness, ataxia, confusion, hallucinations, dizziness, lightheadedness, paresthesia, anxiety, tremor, insomnia, nightmares, weakness, drowsiness, irritability, malaise, lethargy, ileus, jaundice, gastrointestinal bleeding, C. difficile associated diarrhea, pseudomembranous colitis, pancreatitis, hepatic necrosis, intestinal perforation, dyspepsia, epigastric or abdominal pain, vomiting, constipation, oral ulceration, oral candidiasis, mouth dryness, anorexia, dysphagia, flatulence, thrombophlebitis, burning pain, pruritus, paresthesia, erythema, swelling, arthralgia, jaw, arm or back pain, joint stiffness, neck and chest pain, achiness, flare up of gout, renal failure, intarstitial nephritis, hemorrhagic cystitis, renal calculi, frequent urination, acidosis, urethral bleeding, polyuria, urinary retention, gynecomastia, candiduria, vaginitis, Crystalluria, cylindruria, hematuria, and albuminuria have also been reported, respiratory arrest, pulmonary embolism, dyspnea, pulmonary edema, respiratory distress, pleural effusion, hemoptysis, epistaxis, hiccough, anaphylactic reactions, erythema multiforme/Stevens-Johnson syndrome, exfoliative dermatitis, toxic epidermal necrolysis, vasculitis, angioedema, edema of the lips, face, neck, conjunctivae, hands or lower extremities, purpura, fever, chills, flushing, pruritus, urtigaria, cutaneous candidiasis, vesicles, increased perspiration, hyperpigmentation, erythema nodosum, photosensitivity. Allergic reactions ranging from urticaria to anaphylactic reactions have been reported. Also experienced were decreased visual acuity, blurred vision, disturbed vision (flashing lights, change in color perception, overbrightness of lights, diplopia), eye pain, anosmia, hearing loss, tinnitus, nystagmus, a bad taste, agranulocytosis, prolongation of prothrombin time, and possible exacerbation of myasthenia gravis, change in serum phenytoin, postural hypotension, vasculitis, agitation, confusion, delirium, dysphasia, myoclonus, nystagmus, toxic psychosis, constipation, dyspepsia, flatulence, hepatic necrosis, jaundice, pancreatitis, pseudomembranous colitis. (The onset of pseudomembranous colitis symptoms may occur during or after antimicrobial treatment.), agranulocytosis, hemolytic anemia, methemaglobinemia, prolongation of prothrombin time, elevation of serum triglycerides, cholesterol, blood glucose, serum potassium, myalgia, possible exacerbation of myasthenia gravis, tendinitis/tendon rupture, albuminuria, candiduria, renal calculi, vaginal candidiasis, anaphylactic reactions, erythema multiforme/Stevens-Johnson syndrome, exfoliative dermatitis, toxic epidermal necrolysis, anosmia, taste loss.

PART IV: EVOLUTION OF RECOVERY

20. IF YOU SUFFER AN ALLERGIC REACTION

(It is a complete incompatibility between your body and the drug)

If you are allergic to quinolones, as soon as you take a few pills or even one single dose, your body reacts negatively according to the patterns of a so called anaphylactic shock and is not covered by this article, you will need emergency treatment and to stop the drug immediately.

21. EXPECTED EVOLUTION FOR A SEVERE REACTION

This report deals specially with SEVERE reactions. For everyone with a body weight around 160 lb or less there is an extremely high risk of experiencing a SEVERE reaction for doses of fluoroquinolones of 1.500 mg of ciprofloxacin (or its equivalent potency of other quinolones) per day for 7 days or 1.000 mg for 2 months.

Severe reactions are very distinctive because they are extremely long lasting and feature many permanent lesions, especially in the 5 following groups:

- neuropathies, including peripheral, central (insomnia, ...) and autonomic (heart, intestines, ..)
- dry syndrome damages (eye, sinus, ears, skin, mouth)
- cartilage destruction, joint and muscle pains
- vision lesions (floaters, blank points, retina degradation)
- organ damage (liver, kidney, pancreas, lymphatic system)

For a severe reaction, the most probable pattern of evolution consists of feeling early disorders of medium or high intensity, reduced to a group of a few symptoms, and from then on the whole state of the floxed person will worsen for many months until reaching a peak of damage. Some people feel very bad at the middle of the drug treatment, which prompts them to stop it, thus saving a lot of further trouble for them. Others feel bad after really long treatments of 4 or 6 weeks of 1,000 mg daily (always referenced to the potency of ciprofloxacin). Normally those persons took quinolones before for shorter periods and they all thought they had worked fine. Later, they discovered that they had experienced those mild inconveniences pointing to a reaction, but they had never linked both things, symptoms and antibiotic. This latter group of people tends to be hit very strongly because their higher tolerability to the drug allows them to take a lot of it before they get strongly hit.

The most noticeable symptoms have already been explained above.

If according to table 5 your profile after 6 or 9 months after drug cessation resembles a severe reaction and half or more of the symptoms are very intense, then you probably are suffering a SEVERE reaction and this report is especially devoted to such cases. The evolution of the pathology is very characteristic of this syndrome. For severe reactions, new symptoms keep emerging for up to nearly two years after the last pill has been ingested. The worst disorders become apparent between months 6 to 9, but others still appear up to month 20. It varies a lot with each individual, but very typically it evolves as follows:

Month 1-2: (acute phase) maximum musculoskeletal symptoms; possibly crutches or wheelchairs needed, high level of pain, and crippling limitations.

Month 6-9: (acute phase) maximum damage, irrespective of symptoms. Maximum vascular damage, that affects eyes, joints, heart, ears, and so on. Erosion of cartilages can be felt and also diagnosed by physical examination and imaging.

Month 9-30: Increasing of symptoms, people are very much affected all over. Pains all over, with soreness, stiffness. Strong feeling that something is going very wrong. New symptoms of a toxic systemic vasculitis (see later) may arise, like dry eye, dry sinus, and abnormal reactions to otherwise normal infections like flu or colds that lead to a trail of deeper symptoms. If dry eye syndrome does not develop or if it is not long lasting, the chances of overall recovery seem to be far greater. Very intense neuropathies in legs and other areas of the body that can be detected in ordinary testing. Maximum muscle pains.

Month 24-36: Cycling of symptoms. Some disorders may experience an improvement with insomnia and some central nervous system issues. Panic attacks tend to stop. Still very sensitive to any food or supplement with vaso-constrictive properties. Somewhat better from myalgic pains and stiffness towards the end of year three. Still present are exercise intolerance, dry mucous syndromes, and vision lesions.

Month 30-40: Recovery predominant, slow progress but firm. You can feel strong and determined and your spirit might go up too. You start to see what permanent lesions the quinolones have caused. Less neurological pains but still twitching, fasciculations, trembling, itching and other similar symptoms. Less stiffness and soreness, less range of movement limitations as the muscles start regaining some strength. Little or no photophobia; floaters less prominent but still present. Heart arrhythmias gone.

Month 36-60: In roughly 40% of the cases, noticeable recovery for sedentary people (recovery is not complete but normal inactivity prevents the endurance damage from showing up). Slow recovery for active people because strenuous exercises make symptoms reappear; endurance is still low, and the body is not still able to recover normally after physically demanding activity. In the remaining 60% of the severe cases, by month 36 people feel better than a year before but are still far away from recovery.

From the 4th year on: depending on the individual, near complete or partial recovery is reached. Typically irreversible damages include dry eye, dry sinus, dry ears, dry skin, floaters, blank points in vision, some palpitations, liver and pancreas lesions, neuropathic pains-bearable, soreness, stiffness, cartilage erosions, exercise intolerance and occasional muscular pains.

Total recovery time: ranging from up to 3 to 6 years or never in some cases that end up with different permanent lesions.

22. EXPECTED EVOLUTION FOR AN INTERMEDIATE REACTION

Symptoms from a quinolone antibiotic intoxication of a lesser intensity start with mild pains during the treatment or soon afterwards, that are of small intensity and can even pass unnoticed. In any case, during the first months, most of the problems are musculoskeletal and tend to resolve without complications. All the rest of the symptoms can be present. But some six to fourteen months after cessation of quinolone antibiotic therapy, the active athlete can become suddenly prostrated and severely affected, normally in one single or a very few joints.

Month 1-12: Minor musculoskeletal symptoms; limited activity, incorrectly associated with overuse, or mechanical problems. Acute phase for other minor effects.

Month 12: (Acute phase, for active, athletic people only) due to accumulated damage, peak symptoms are reached. Collapse of a joint is typical. There are no or very mild accompanying symptoms (vision, neurological, etc...).

Month 12-22: Recovery predominant, relatively fast progress.

Active and athletic people will see their endurance drop a lot and they will develop osteoarthritis early, perhaps some ten years earlier than non-floxed people, and depending on dosage.

23. EXPECTED EVOLUTION FOR A MILD REACTION

In these cases, apparently there are no symptoms associated with the quinolone treatment and the individual can feel no adverse reactions after taking a quinolone prescription, especially a short one or one with low doses. But the quinolone takes its toll and after several treatments spaced weeks, months, or even years apart, subtle symptoms will begin to develop, and the sufferer will probably never link them to the antibiotic.

These symptoms will probably be: restlessness, especially at night, brain fog, some minor twitching, increased coolness of hands and feet, slower recovery after strenuous activity, increased stiffness after exercise. And the unavoidable erosion of cartilages will be inevitably added to the list.

In short:

Severe reactions present themselves with intense, long-lasting joint and neuromuscular symptoms as well as eye disorders and dry mucous parts.

In MILD reactions, recovery is reached between months 4 and 12 on average. In some cases they have an acute phase of up to 3 months.

24. WHICH KIND OF ADVERSE REACTION TO QUINOLONE ANTIBIOTICS ARE YOU SUFFERING FROM?

Reactions to drugs vary among individuals. But there are some very common patterns of bodily responses to quinolone intoxication. First of all, you should discern among:

- ACUTENESS. Some reactions are sudden and very acute, causing a lot of distress to their sufferers, but they resolve in a few months because the reaction has manifested abruptly but not deeply.

- SEVERITY. Other reactions have a medium intensity of symptoms at onset but they insidiously develop progressively to very severe reactions over time (usually 12 or 18 months).

In other words, a person suffering from QTS (QUINOLONE TOXICITY SYNDROME) **cannot infer from his/her initial symptoms** what kind of reaction he/she is experiencing.

Many people suffer acute reactions during the first days. Even though they get very scared the acuteness has no direct relation with the severity of the reaction as a whole. You will only be in a position of making a judgement on the severity of your QTS after a few months after the cessation of the drug, when you line up the whole list of symptoms, their intensity and their evolution.

From the study of many cases we have concluded that is useful to create a simple scale of severity of the reactions: MILD, INTERMEDIATE and SEVERE. We do not take into account the acuteness of the initial reaction, because it has been proved that it has no relationship with the evolution of the QTS. According to this scale you can end up having a mild, intermediate or severe reaction. Obviously there are no clear delineations between them and every reaction is unique and personal, but if you can assess as to which kind you are experiencing, you will acquire a more precise diagnosis and will be able to address your problem accordingly.

If you suffer a MILD reaction you can expect a good recovery in 4 or 6 months. For an INTERMEDIATE reaction, typically there is a convalescence of 1 to 2.5 years with a diminished but acceptable life quality. SEVERE reactions mean a miserable living for at least 3 years plus another 2 years to get acceptable pain levels, ending up with permanent lesions and life limitations. Remember that this article focuses primarily on severe reactions.

Everyone behaves slightly different to the floxing because daily habits and personal conditions can somewhat modify the evolution of the recovery.

Check whether you fall into one of the following categories. On top of that everyone is different and can have, for example, 20 symptoms belonging to the intermediate reaction level, and 1 or more with a greater intensity, typical of a severe reaction.

| -TABLE 5- INTENSITY OF SYMPTOMS AT THE END OF MONTH 6 POST-FLOXING FOR DIFFERENT LEVELS OF REACTION | | | |
|--|-----------------------------|-------------------------|------------------|
| SYMPTOM | if you are suffering from a | | |
| | SEVERE REACTION | INTERMEDIATE REACTION | MILD REACTION |
| joint pains, arthritis, osteoarthritis | severe | limiting | mild |
| generalized pains | intense, growing | no | no |
| tendinitis | widespread | limited to a few places | mild, localized |
| soreness, stiffness | high | medium | mild or none |
| recovery of physical traumas | impeded | normal | normal |
| skin lesions, rash | common | some times | no |
| cool hands/feet, poor circulation | very intense | some degradation | no |
| brain issues | yes | no | no |
| depersonalization, panic attacks | very common | usual | not usual |
| twitching, numbness, tingling... | severe | noticeable | unnoticeable |
| insomnia, anxiety, brain fog | universal, intense | very common | common, but mild |
| vision (floaters, lights, blank points) | very common | uncommon | unusual |
| photophobia | universal | common | uncommon |
| focusing problems | possible | uncommon | no |
| impotence | increasing | no | no |
| sensitization to foods, chemicals, odors | very common | uncommon | no |
| dry sinus, dry eye, dry ear, dry skin | yes | no | no |
| neurological spasms | yes | no | no |
| heart palpitations, arrhythmias | worsening | occasional | possible |
| elevated serum enzymes and titers | yes | no | no |
| tinnitus, ringing in ears | frequent | sometimes | unnoticeable |
| peripheral neuropathies | universal, worsening | common, limited | unusual |

The entire list of the adverse reactions to a typical quinolone is included in another section of this report.
For a more precise diagnostic, the comparative study of symptoms should be done at the end of month 6.

| -TABLE 5-cont'd- EVOLUTION OF THE SYMPTOMS (see later in the article) | | | |
|--|----------------|----------------|--------------|
| new disorders appearing or increasing | up to month 18 | up to month 10 | unnoticeable |
| peak point of disorders (downturn) | at month 20 | at month 12 | early months |

In fact, it is the CRITICAL ISCHEMIC POINT that distinguishes between severe and non-severe floxings. This is, by definition, the level of toxicity that provokes an overall ischemia (narrowing, flood depriving of blood vessels) all over the body, in such a way that ANY small increase in vasoconstriction sharply worsens the condition of the floxed person. This vascular implication is explained later.

In mild and intermediate floxings, the ischemia of the blood vessels has not reached its critical point and still can endure more narrowing before more nerves and tissues start to massively die off. However, in severe floxings the critical point of ischemia has been surpassed and there is not any margin left for further vasoconstriction, and therefore small amounts of foods, substances, or actions that induce even more narrowing of the vessels cause immediate pains in nerves, exacerbation of vision issues, and many more relapsing symptoms.

Mild and intermediate reactions cause more concentrated lesions, especially neurological, and other smaller disorders. Severe reactions cause massive disturbances all over the body, as the entire network of nerves and organs are damaged, and some cannot heal properly, so the medical picture is overwhelming.

Severe reactions have a much worse prognosis (likely future outcome) than the rest. For a rapid evaluation, the main characteristics of a severe reaction are:

- 1) *caused by long or high dose treatments (6 weeks of 2x500mg daily or 1 week 2x750 mg daily of cipro)*
- 2) *symptoms increasing or emerging after month 6*
- 3) *dryness syndromes (eye, sinus, ear, mouth) that do not clear up by month 14th or so*
- 4) *multiple joint and muscle pathologies*
- 5) *general stiffness and inability to gain muscle mass no matter how much exercise is done*
- 6) *extraordinary soreness a few hours after attempting vigorous exercise*
- 7) *constant pains already present on waking up instead of increasing during the day*
- 8) *vision floaters and flashing lights*
- 9) *reactions to foods and over the counter drugs that you did not have before*
- 10) *cold hands that persist in normal situations, with poor blood circulation*

If you have the first two plus another 5 or more of these afflictions and they are intense, then you probably are suffering from a severe reaction.

Summarizing:

Many reactions are mild and intermediate and heal in a few months or years with no serious sequelae, but only after a lot of suffering.

25. WHAT ARE YOUR CHANCES OF RECOVERY?

As explained before, most people recover from the quinolone intoxications. Many do not. Everyone with intermediate and severe reactions sustains permanent damage although it can be internal and it can remain more or less unnoticed if it does not affect their daily lives much (cartilages, central nervous system). Some people end up with permanent chronic pain, physical difficulties, heart or vision damage, and many other irreversible lesions.

Therefore, if the toxicity level is not high, that is to say, if there are little nervous and vascular system alterations, the average person will probably recover, albeit with the cartilages of the weight bearing joints slightly eroded. The athlete will enter an accelerated course of decay because his/her cartilage will not keep up. The endurance athlete will no longer be able to perform at a decent normal level.

For instance, in severe cases photophobia resolves in some two years on average, focusing impairments in 2.5 years, and flashies and floaters take many years to fade off. Another indicator of the severity of the floxing is a dry mucous condition. If you have long-lasting dry eyes, plus dry mouth and sinus, you are no doubt suffering a severe reaction and running the risk of ending up with permanent lesions.

If the toxicity level is high, the average person might eventually get a decent daily life similar to the one he or she enjoyed before taking a quinolone, but with some physical limitations for repetitive and strenuous activities. The athlete will no longer be able to return to competition in any impact sport, and in the best case he will be capable of enjoying biking, hiking, swimming or other sports that put little stress on the joints. Healing and recovery time until reaching this point is more than three years on average. There is a concerning number of cases for which recovery seems to be elusive after five or more years after the last quinolone pill ingested. Perhaps during the coming years we will see the confirmation of a vast number of cases of permanent disability, or lifelong pains and misery caused by quinolone antibiotics.

Chances of recovery are predominant for the age bracket of 20-40 years. After the age of 40 recovery can take much longer. Beyond the fifties more permanent damages are recorded. For people above 70 years old, recovery is completely unlikely in the case of severe reactions.

Nearly all floxies can tell when they are recovering, because at a precise point in time they begin to experience less problems with foods (recovery of the toxicity and neuropathies that prevent intestines and organs from working properly), a lower level of pains, less stiffness and soreness, more flexibility, there is a weight gain, insomnia improves, and they feel stronger in every sense. Then

some anxiety develops in all floxed persons because they all see a glimpse of normalcy on the horizon, and would like their ordeal to stop immediately after long years of suffering. But in severe floxings, on average, you feel some recovery when you are halfway through the reaction, that is to say, at the 2.5 year mark for a 5 year recovery period. The second part of the floxing is more compatible with a normal life (except for sports or strenuous activities) but you still cannot eat freely, you endure many periods of cycling, and many neuropathies and permanent lesions (vision; eye, ear, and skin dryness) are still present and the floxed person gets concerned about the quality of life already lost and the perspectives lying ahead.

It is summarized as follows:

| -TABLE 6- LIFE AFTER RECOVERY | | | |
|--|-----------------------------------|--------------------------------|-------------------------------|
| | reaction that you suffered | | |
| | SEVERE REACTION | INTERMEDIATE REACTION | MILD REACTION |
| average recovery time | 5 years, or never | two years | months |
| permanent damage | frequent | uncommon | no |
| ISSUE | DISORDERS AFTER 5 YEARS | DISORDERS AFTER 2 YEARS | DISORDERS AFTER 1 YEAR |
| joint+muscle pains | occasional | no | no |
| cartilage erosions, early osteoarthritis | permanent | common | no |
| decreased endurance | permanent | permanent | no |
| stiffness of joints and limbs | common | uncommon | no |
| vision (floaters, ziggies, flashies, blank points) | common | no | no |
| photophobia | no | no | no |
| focusing problems | no | no | no |
| insomnia, anxiety, brain fog | no | no | no |
| depersonalization, panic attacks | no | no | no |
| heart palpitations | occasional | no | no |
| numbness, tingling, twitching | occasional | no | no |
| tinnitus, ringing in ears | occasional | no | no |
| peripheral neuropathies | very common | no | no |
| sensitivity to foods, chemicals and substances | common | no | no |
| <i>this table shows the expected sequelae of a floxing on a healthy young individual</i> | | | |
| <i>"occasional" means that you will notice it occasionally</i> | | | |
| <i>"permanent" means that you will suffer it for life</i> | | | |
| <i>"common" means that the issue is still common after 5 years</i> | | | |

The successful recovery stories of people enduring intermediate and mild reactions are currently overrated because many people that end up feeling normal are still far behind a complete recovery but they cannot tell because they are sedentary. Those persons can report that they are cured some two years earlier than the real healing takes place. Nobody really gets out undamaged. Although it is difficult to trace enough people long enough to get a conclusion, it is widely admitted nowadays that many people remain symptomatic in a permanent, irreversible manner.

Remember:
 If you suffer a severe reaction, your chances of complete recovery are lower than 40%.

PART V: VASCULAR DAMAGE

26. THE VASCULAR CONNECTION

This area of the report is a hypothesis on the ultimate cause of the floxing syndrome. We cannot aim to discover anything of medical importance. But we can argue about some ideas that correspond well with our experiences, the clinical symptoms that allow us to favor some habits and avoid others in our daily lives, with some basic understanding about the why and why not.

Although it is not generally accepted, we think that one of the main damaging paths used by fluoroquinolones is vascular. There are many scientific papers that relate vasculitic events induced by quinolones but they are presented as exceptional or rare happenings. However, the quinolones unfailingly provoke a specific sort of vascular lesion(s).

Arteries are composed of 3 layers. The intima is composed of the endothelium and underlying subintimal connective tissue. The media is composed of the internal and external elastic lamina surrounding the smooth muscle. The adventitia lies at the outermost area comprised of connective tissue in which nerve fibers and vasa vasorum (small vessels) are dispersed.

The vasa vasorum exist within the substance of the end organs. These vasa vasorum include the capillaries, that are approximately the size of a red blood cell and they do not have the media layer. The very small vessels that surround and supply the nerves are called vasa nervorum.

The quinolone antibiotics either alter the capillaries permeability, or induce the deposition of immunological complexes inside them, or cause a spasm-like narrowing of their ducts. In any case, the result is the same: muscles, skin, nerves, heart, brain and other organs are deprived of blood flow (ischemia), and they die or do not work properly. Therefore, in this report we define vasculitis as an inflammation of the vessel walls with vascular damage or attendant tissue injury.

What nobody knows and requires much more research are the factors that determine the duration of disease, the type of tissues involved and their damage, as well as how to target therapies at inflammation without interfering with healing.

Accumulation of inflammatory cells in the vessel wall is the common feature of vasculitis, although it is not well understood how tissue damage occurs. It is widely admitted that there is a three-stage process:

- initiation of the injury
- recruitment of inflammatory cells and tissue damage
- regulation of the immune response.

Quinolone vasculitis is a systemic vasculitide (so called because of its multi-organ nature). Inflammation and damage can be transient or more permanent. The alterations in coagulation and vasomotor tone result from local damage to the endothelium as well as intrinsic components of the cytokines that are released through the process. Drug toxicities are among the causes and processes strongly associated with vascular injury. Immune complexes with certain immuno-chemical characteristics activate a complementary cascade that induces neutrophil mediated damage to the vessel wall. The presence of granulocytes is usually associated with fibrinoid necrosis as would be expected on the basis of their release of toxic enzymes during inflammation. Necrosis in the vessel wall is a large contributor to scarring and the delayed sequelae present in some cases of vasculitis, such as the quinolone-induced vasculitis.

Normally, quinolone vasculitis appears some time after exposure, and is a link in the chain of adverse events that take place for months on end. All of the vasculitides are likely secondary to some form of inflammatory stimulus, usually infectious or toxic, as in our case. In quinolone vasculitis the real underlying cause either cannot be identified (no doctor is willing to admit that quinolones are the direct cause of vascular disorders) or has long since been cleared by the host, leaving only a chronic or recurrent inflammation focused on the vasculature.

Toxins as a cause of vasculitis are increasingly established. Overall, vasculitis secondary to a defined infection or toxin is clearly the most frequently encountered vasculitis and an important etiology in peripheral nerve vasculitis. Because quinolone vasculitis is so varied in its presentation and clinical pace, early identification may be difficult. In this vasculitis, neuropathies are frequent, occurring in 80%-100% of patients. Mono-neuropathy multiplex is the most distinctive pattern in intermediate reactions to quinolones, although nerve alterations of other kinds are very common as well (twitching, throbbing, pins and needles, numbness, sensory poly-neuropathies). See the paragraph devoted to neuropathies.

Then, there is the issue of diagnosis. The diagnosis of vasculitis is fundamentally an invasive process (biopsy). A critical feature is the identification of inflammatory cells that diminish the delivery of blood to tissue. Furthermore, the numerous causes that may

result in vasculitis can often be distinguished only at the cellular level. Histological studies characterizing lesions on the basis of the infiltrating cells may provide information on both the mechanisms inducing inflammation and predict the sequelae of the lesions. There is an urgent need to determine the underlying mechanism for appropriate treatment.

For most floxed persons the blood studies may be entirely normal. There is no serological test that confirms or excludes a vasculitis. Quinolone vasculitis is:

- seronegative (non-ANCA, negative SSA, SSB, anti-Sm, normal anticardiolipine, antiphospholipid, soft muscle markers, halotypes....)
- drug-induced, non-abating with drug withdrawal, and typically reaches its acute phase many months after drug discontinuation, when the ischemic process has managed to kill enough nerves or cells.
- not responsive to any known treatment; very long lasting or permanent, because many nerves die and cannot be regenerated.

Being non-ANCA, the floxing vasculitis is normally classified by some advanced doctors as drug-induced immuno-complex vasculitis that shares similarities with other immuno-complex vasculitides like systemic lupus erithematosus, rheumatoid arthritis and Sjögren's disease.

In summary, blood ducts extend in smaller and smaller conducts, called arterioles and venioles. The real ends of them reach every part of the body and the red blood cells have to circulate through them almost in single row. The former ducts bring the oxygen and the nutrients and the latter ones collect the by-products and CO₂ (carbon dioxide) resulting from cell activity.

There are zones with very little arteriole and veniole supply: cartilages, tendons, nerves and connective tissue. Due to the vasculitis caused by quinolones, the inner diameter of the conducts is narrowed. The result is that the vessels cannot correctly supply the tissues or take away the waste. The consequences are:

- lack of blood supply (injury to vasa nervorum) in nerves that cause intense neuropathy-like numbness, tremors, twitching, tingling, neuritis and dying of nerves, escalating the pain response and perpetuating the lesions.
- lack of blood supply to cartilage, in addition to the toxic assault, causes necrotizing, and erosion with osteoarthritis in weight-bearing joints.
- lack of blood supply in tendons and overuse with daily movements causes tendinitis.
- heart arrhythmias, palpitations, poundings, that last for years and in some cases require the implantation of a pacemaker. Many deaths have been associated with quinolone-induced cardiopathies.
- poly-myositis and muscle destruction are frequently seen in severe reactions.
- lack of blood supply in the extremely narrow ocular vessels causes sparkling, zig-zagging, wandering small lights. Floaters are a result of dying cells due to lack of blood supply. Many floxies get ischemic areas in the outer margins of the retina. Optic neuritis is very common.
- temporary and complete loss of vision, occurring in some cases from month 5 to month 13th: lack of irrigation of the eyes.
- lack of blood supply near the skin in the more distant areas of the body and a tendency to have cool feet and hands

This vasculitis seems to be an autoimmune disease and, according to many medical reports, mild reactions are responsive to most conventional treatments such as corticosteroid therapy, immunosuppressive drugs, and the like. In the case of a severe reaction, long-term treatments with corticoids are contraindicated (increase very much the likelihood of experiencing a tendon rupture) and also ineffective.

The search for a non-invasive marker for vasculitis remains disappointing. Some of the most effective treatments for quinolone-induced toxicity are substances with a strong vaso-dilation activity or active blood thinners. On the other hand, substances with vaso-constrictive properties are nearly always detrimental for floxed persons and induce relapses, an increase of symptoms and delayed recoveries.

Remember:

Your problems after the reaction are the tip of the iceberg. The quinolones have damaged all your body systems to different degrees.

There is a specific disorder caused by quinolones, especially ciprofloxacin, (and other antimicrobials as well) called haemolytic anemia. The drug (i.e. cipro) attaches to some proteins in the body (creating an immuno-complex) and targets the surface of the erythrocytes (red blood cells) causing the blood to clog in certain situations, especially in low temperatures. Then, much cold is felt in hands and feet and in some other areas of the skin because the clots block the blood flow through the very narrow small vessels of the affected areas. For average temperatures, the immuno complex detaches from the red cells and no clots are formed, because both the complex and the red cells circulate separately.

There are some tests to check the extent of the affliction by a potential haemolytic anemia, including the Coombs test and others that many doctors are aware of.

27. VASCULITIC RASHES

Many severe cases of intoxication by quinolones have a skin rash present. There is a predilection for the distal ends of the limbs: hands and feet. The following picture is an example of a vasculitic rash induced by ciprofloxacin in a young athlete.

These rashes tend to resolve spontaneously, but signal serious reactions to quinolones.

In all, about 15% with severe or intermediate adverse reactions to quinolones actually develop a vasculitic rash.



*-Picture 1- The points marked as "B" are red points, like pustules but with no secretion.
The point marked as "C" is a purple type of hematoma.*

PART VI: NEUROLOGICAL DAMAGE

28. NEUROLOGICAL IMPLICATIONS

The longest lasting damage from quinolones are perhaps the neurological alterations. Neurotoxicity is a common feature of all quinolones since such adverse reactions have been described with all quinolone derivatives to date. Some research suggests that they are due to the neuromuscular blocking effects of quinolones. Maybe they are secondary (a consequence) to the vasculitic mechanism. Neuropathies are a prominent feature of the toxic vasculitides. The reasons for this frequency are not immediately clear. The rich blood supply and the capacity of nerves to function reasonably well with anaerobic (no oxygen) metabolism normally render the nerve relatively resistant to ischemia (disruption of blood supply). That is a reason for delayed symptoms. The immediate cause of the vasculitic neuropathies is inflammation or deposition of immuno-complexes that eventually harden, thicken, and develop scar tissue, thus decreasing the diameter and impeding blood flow with occlusion of the vasa nervorum, resulting in ischemia of the peripheral nerves that end up damaged or dead. This category of nerve damage, in which isolated nerves in different areas are damaged, is called mono-neuropathy multiplex or multi-focal mono-neuropathy.

In addition, nearly all the floxed persons have peripheral neuropathy. Peripheral neuropathy describes damage to the peripheral nervous system, the vast communications network that transmits information from the brain and spinal cord (the central nervous system) to every other part of the body and vice versa. Because every peripheral nerve has a highly specialized function in a specific part of the body, a wide array of symptoms can occur when nerves are damaged. Some people may experience temporary numbness, tingling, and pricking sensations (paresthesia), sensitivity to touch, or muscle weakness. Other floxed persons, particularly in severe reactions, may suffer more extreme symptoms, including burning pain (especially at night, very exacerbated by heat), muscle wasting, paralysis, or organ/gland dysfunction. People may become unable to digest food easily, maintain safe levels of blood pressure, sweat normally, or experience normal sexual function.

Some forms of neuropathy involve damage to only one nerve and are called mono-neuropathies that in many cases are difficult to recognize properly and are then diagnosed as normal musculoskeletal lesions. Sometimes two or more isolated nerves in separate areas of the body are affected, called mono-neuritis multiplex. Often though, multiple nerves affecting all limbs are affected, called poly-neuropathy. Toxic drug-induced neuropathy usually involves nerves on both sides of the body, although not always symmetrically (many floxed persons become far more rigid and/or stiff and have more pain on one side), and pain is a common symptom. The neuropathies floxed persons experience are predominantly asymmetrical and they migrate around certain areas of the body, with a marked predilection for lower limbs (large myelinated axons) and distal areas (hands, feet).

In short, quinolones damage both the central and peripheral nervous systems. It is very typical to feel pins and needles sensations, as well as throbbing pains, numbness, trembling, fasciculations (crawling under the skin), tremors, twitching, and neurological pains migrating all over the body. In most severe floxings the associated pain typically does not respond to simple analgesics, and can become chronic and may interfere with sleep (more intense in hot areas of the body) and also be present at rest. Neuropathic pain is difficult to control and can seriously affect emotional wellbeing and overall quality of life. As has been shown earlier: insomnia, nervousness, anxiety, overreactions to stress, anger and anguish are also very common.

The damage is very extensive and symptoms fit well in many neurological sub-diseases, like all kinds of peripheral neuropathies: mono-neuritis multiplex, sensory-motor neuropathies, demyelinating neuropathies, axonal neuropathies, autonomic nerve damage, and many more specific disorders. Central nervous system neuropathies affect many organs like the heart, eyes, brain and intestines.

The main problem with this toxic neuropathy is that recovery for severe reactions is often only a partial recovery.

29. PERIPHERAL NEUROPATHY

Peripheral neuropathy affects a variety of peripheral nerve cells and fibers, including sensory (temperature, touch, vibration...), motor (muscles), and autonomic (orthostatic pressure, erection) fibers. Most quinolone induced peripheral neuropathies affect all fiber types to some extent. However, a single fiber type may be predominantly or exclusively affected in some cases producing very particular neuropathies. In some floxed persons, peripheral neuropathies involve single peripheral nerves (single=mono neuropathies), or numerous individual peripheral nerves, the so-called mono-neuritis multiplex syndrome. In addition, peripheral nerve disorders may involve the brachial plexus, lumbosacral plexus, or a single root, that is to say, the low spine, resulting in signs and symptoms in one limb, with pains that can be excruciating. Most cases of floxing conform to a poly-neuropathy syndrome,

which usually implies both sensory and motor fiber involvement in a relatively symmetric fashion and typically with a distal-to-proximal gradient of involvement (more intense the more distant from the trunk). These conditions are termed sensory-motor polyneuropathies, and they represent the most common form of peripheral neuropathy. They also cause a diminished quality of life.

Quinolones can induce pathologic reactions in the nerves: wallerian degeneration, axonal degeneration, and segmental demyelination. In wallerian degeneration, the axon degenerates distal to a focal lesion that interrupts the continuity of the axon. This reaction often occurs in focal mono-neuropathies that result from nerve infarction as a result of an ischemic vasculitic process. The toxicity plus the ischemia interfere with nerve metabolism. They affect the longest neurons first, since long neurons have greater metabolic demands than short ones. Symptoms therefore may begin in the feet, then progress up the legs and then affect the hands. It is a typical pattern of severe reactions. In intermediate reactions the neuropathy does not usually progress up.

Axonal (rod) degeneration starts at the most distal (distant from the trunk) extent of the axon. Axonal degenerative polyneuropathies are usually symmetric (although frequently with different pain intensities in both sides), and are the most common in flogings. Floxed persons also predominantly show signs of segmental demyelination that refers to focal degeneration of the myelin sheath with sparing of the axon. This reaction can be seen in focal mono-neuropathies but also in generalized sensory-motor or predominantly motor neuropathies. Toxic segmental demyelinating polyneuropathies might be the result of the immunological reaction.

In those peripheral nerve disorders that are characterized by either wallerian degeneration or axonal degeneration, prognosis (likely outcome) is less favourable due to the fact that the axon must regenerate and re-ennervate muscle, the sensory organ, blood vessels, and other structures before clinical recovery is noted. That is why the new warning (October 2004) in the package insert of quinolones mentions "irreversible condition". Recovery may be more rapid with segmental demyelination because remyelination is accomplished more quickly, in turn re-establishing normal conductivity of the axon and return of function.

It is easy for the floxed person to feel and describe the multiple symptoms of his/her peripheral neuropathy.

Sensory symptoms: Sensory symptoms include sensory loss, a sense of numbness, tingling, prickling, and pins-and-needles sensations, pain, thermal sensation, vibratory sense and intolerance to light touch. Damage to large sensory fibers lessens the ability to feel vibrations and touch, resulting in a general sense of numbness, especially in the hands and feet. People may feel as if they are wearing gloves and stockings, or having the foot in a cast. In most generalized polyneuropathies, these symptoms begin in the most distal (far from the trunk) extent of the longest sensory fibers, like the toes and feet and then crawl their way up to the knee point in which the disorder also starts at the fingertips spreading the process to the upper extremities. In addition to sensory loss, patients frequently complain of paresthesias and dysesthesias, often characterized by a sense of numbness. Pain is a serious symptom for many floxed persons. It may be described as a dull aching sensation, an intense burning sensation or, occasionally, as intermittent lancinating pulses of pain (called 'throbbing' in this report).

Motor-muscle: Muscle weakness is the most common symptom of motor nerve damage. All severe reactions present with a loss of muscle mass that cannot be recuperated irrespective of how much exercise or workouts are done. Other symptoms may include painful cramps and fasciculations (uncontrolled muscle twitching visible under the skin), muscle loss, bone degeneration, and changes in the skin, hair, and nails (these more general degenerative changes also can result from sensory or autonomic nerve fiber loss). Impairment of motor function typically begins with weakness in the toes, and as the polyneuropathy progresses, ascends up the distal lower extremities to the level of the knees, at which time motor involvement in the hands may be observed.

In the toxic segmental demyelinating polyneuropathies, proximal muscle (quads) weakness resulting from root (polyradiculoneuropathy) involvement may be observed. Axonal degenerative polyneuropathies tend to produce weakness along with muscle atrophy, but atrophy is much less conspicuous in segmental demyelinating polyneuropathies because in these disorders the axon remains in continuity with the muscle, preventing denervation atrophy. Therefore, your doctor can measure the perimeter of your thighs and tell you that he/she finds both the same size, even though you feel your more painful one nearly useless, soft, idle and deprived of strength. A common symptom (but not universal) in severe flogging polyneuropathy is weakness in dorsiflexion of the big toe. That disability is somehow a measure of the initial severity of the mono-neuropathy of the distal peroneal, tibial and flexor groups of the lower leg, and progresses up for severe reactions to weakness of quads or even gluteus in the worst cases.

Motor toxicities have a much deeper influence in the health of floxies than is normally acknowledged. Motor nerve injuries caused by quinolones provoke a lack of function of the related muscles, and they become atrophic. The atrophy makes the limb to work improperly and other muscles and nerves are overstressed, causing further pains, sometimes very intense for many years. The bad news is that some of this motor nerves have a limited capacity of healing, and normally they also have deadlines for healing (around 2 years) after which time they cannot recover and the injuries and pain cannot be reversed apparently.

Autonomic nerves: Some floxies report symptoms that indicate that autonomic fibers are also affected. Symptoms of autonomic nerve damage are diverse and depend upon which organs or glands are affected. Autonomic nerve dysfunction can become life-threatening when the heart begins beating irregularly (extremely common in floxed persons)

or there is difficulty with breathing. Other common symptoms of autonomic nerve damage include an inability to sweat normally (floxed persons notice reduced or absent sweating in the legs and hands, and at the same time excessive sweating confined to the head and neck region), a partial loss of bladder control and an inability to control muscles that expand or contract blood vessels to maintain safe blood pressure levels. A loss of control over blood pressure can cause dizziness, light-headedness, or even fainting when a person moves suddenly from a seated to a standing position (orthostatic hypotension).

In severe floxings other autonomic symptoms include dryness of the eyes and mouth (another marker of the severity of the floxing) and gastrointestinal dysfunction (nerves controlling intestinal muscle contractions often malfunction), often manifested by alternating constipation and diarrhea or by early satiety. Many people also have problems eating or swallowing if certain autonomic nerves are affected. In intermediate and severe floxings in men, partial erectile dysfunction or incontinence is one of the first autonomic symptoms.

More details on autonomic nerve dysfunction (neuropathy) are treated later on this paper.

Diagnosis. Such a vast array of presentations of peripheral neuropathy in floxed persons makes precise diagnosis a challenging task and is the reason that physicians reach different conclusions depending on the predominance of the axon/myelin, focal/diffuse, symmetric/asymmetric, sensory/motor/autonomic involvement, and adding the difficulty posed by the fact that floxed persons develop all of them to different degrees.

Doctors may order a set of tests to evaluate your disorder: nerve conduction studies, needle electrode examination, brain and spine MRI, lumbar puncture for cerebrospinal fluid analysis. Blood and urine tests can include glucose tolerance test, vitamin B12, serum protein, anti-GM1 antibodies and anti-myelin antibodies, plus investigations of markers of various connective disorders associated with vasculitis. The ultimate analysis is a nerve biopsy, that when performed with the most advanced techniques by well-trained physicians can assist in the complete characterization of the lesions. It is an invasive procedure and few floxed persons have undertaken it because it is mainly ordered only in severe reactions and when a diagnosis of vasculitis or immune reaction of another type is being considered. Less common are precision sensory testings, and studies of sudomotor function, and autonomic responses to provocative physical maneuvers.

In many cases the electrical conductivity tests render normal results, as well as MRIs of the brain and spine, and spinal taps. But it is also very typical that well conducted studies discover alterations in the sensory and motor status of the nerves in many parts of the body. Muscles also show decreased responses in electromyographic (EMG) studies.

Other very common findings are decreased or altered signals in the nerves that control the hands, especially the ulnar nerve. You will know that your ulnar nerves are affected if your small and ring fingers become numb, normally if you exert pressure around your elbow or when bending your elbows sleeping at night. Some doctors will tend to diagnose you as having ulnar or carpal tunnel syndrome, but you are really suffering toxic ulnar neuritis.

Other nerves very commonly implicated are the nerves of the legs. Pains occur predominantly in the hamstrings, lateral or medial knees, outer gluteus, calves, quads, groin, and several areas of the ankle, plus the toes. Many times pains mimic strains, tendinitis, muscular fiber disruptions, and sprains, but they are toxic neuritis.

Remember:

In severe reactions neurological pains can last for years and impair your quality of life.

In general, we have multiple peripheral nerve lesions. They can occur sequentially and in a random fashion (now the upper left leg, then the right ankle, etc...). As stated before, the earliest findings are loss of vibratory sensation in the toes, atrophy of intrinsic foot muscles, and reduced or absent ankle jerks. In severe reactions there are signs of lower motor neuron lesions: weakness, more generalized atrophy and fasciculations. Sometimes fasciculations are referred to as "twitching" and they are a serious symptom of denervation that normally shows up as motor (axonal) nerve damage that is mainly irreversible and can only be recovered through new nerve fiber regeneration.

Double or triple mono-neuritis dominates in intermediate reactions. For instance, the right leg (hamstring and ankle-Achilles) plus heart arrhythmias and perhaps an elbow epicondylitis. Multiple neuritis is more typical of severe reactions. For instance, this includes the right leg, plus heart disorders, plus elbow, shoulder, hips, wrists, and above all- optic neuritis.

Optic neuritis reflects a lesion of the optic nerve and is a secondary effect of the damage caused by the quinolones to the small blood vessel complexes of the eye (in fact is an ischemic optic neuropathy). The optic nerve dysfunction usually manifests with blank spots, difficulties in focusing, and in severe cases transient complete losses of vision with a solid white vision in one or both eyes. These blindness episodes have been reported with ciprofloxacin and last for some minutes, are very terrifying, appear suddenly, so they are also dangerous depending on the activity in which the floxed person is engaged. These events of blindness can happen periodically up to 18 months after the treatment with ciprofloxacin and at any time in the following years if the floxed person experiences a high re-exposure to quinolones through poultry ingestion, for instance.

If the intoxication of the quinolones has been intermediate, these neurological symptoms tend to disappear in two years time on

average. If the intoxication has been severe, the neurological disorders linger on for many years without abating, although in the 4th or 5th year mark the floxed person can experience an improvement.

30. AUTONOMIC NEUROPATHY

Classical presentations are orthostatic hypotension, impotence or ejaculatory dysfunction, decreased sweating, and urinary incontinence. For example, when floxing mimics Sjögren syndrome, dry mouth and eyes along with anhidrosis prevail as initial presentation. In general, common symptoms are:

- Facial - Facial pallor, anhidrosis
- Ocular - Blurring then graying of vision, blacking out, tunnel vision, sensitivity to light, difficulty with focusing, reduced lacrimation, loss of pupillary size over time (which is often correlated with loss of visual symptoms).
- Cardiovascular - Orthostatic onset of palpitations, nausea, tremulousness, presyncope with light-headedness, visual blurring, tinnitus, and even chest pain and shortness of breath
- Orthostatic hypotension. Supine hypertension and a loss of diurnal variation in blood pressure may occur later.
- Episodes of palpitations, angina, dyspnea, and syncope may relate to cardiac arrhythmias as well.
- Gastrointestinal - Constipation, episodic diarrhea, early satiety, increased gastric motility, dysphagia, bowel atony, bowel incontinence, hyposalivation, and altered sense of taste.
- Renal - Nocturia, bladder urgency, bladder frequency, enuresis, incomplete bladder voiding, urinary retention, and urinary incontinence
- Sexual - Impotence (mainly parasympathetic) and loss of ejaculation (mainly sympathetic), retrograde ejaculation, and possibly, female sexual dysfunction
- Sweating - Anhidrosis or hypohidrosis, compensatory hyperhidrosis, gustatory sweating
- Temperature regulation - Hypothermia (from loss of shivering and inability to vasoconstrict to prevent heat loss) and hyperpyrexia (may be of concern to patients with anhidrosis who are exposed to high temperatures)
- Feet - Burning feet most commonly observed in small-fiber sensory neuropathy (itching of feet may precede burning),
- Pruritus, dysesthesia, allodynia, hyperalgesia, nocturnal exacerbation of symptoms, dry skin, loss of distal leg hair, brittle nails, pallor, and cold feet.

In floxings, the common occurrence of arthralgias and pseudo-arthritis, rash, renal disease in very high doses, can suggest to many well trained doctors a connective tissue disorder, such as rheumatoid arthritis, systemic lupus erythematosus, or Sjögren syndrome and therefore one could obtain such diagnosis after the quinolone intoxication.

31. WHAT ABOUT THOSE ANNOYING CRAMPS AND TWITCHING

It is well known and accepted that severe cases of quinolone toxicity are distinctive for the high level of toxic myopathy developed by all floxed persons. But the quinolones have been conceptually sold to the prescribing doctors like the perfect antibiotic when in fact they cause devastating, long lasting (for years, and many times permanent) myopathies and motor neuron disorders. On the other hand, many other drugs have been clearly associated with muscular toxicity (AZT with mitochondrial myopathy; corticosteroids with myosin deficiency myopathy; statins and cyclosporine with rhabdomyolysis; etc...).

A very worrying symptom that many people experience as part of their strong reactions is muscle twitching. Twitching can be of very different types, but could be simply classified as:

- Fibrillations, imperceptible fasciculations, only detectable by electric devices. They are characteristic of inflammatory myopathies and denervation. They are spontaneous action potentials in a single muscle fiber, not visible on physical examination. Physically they last 1 to 5 milliseconds in duration and their firing rate is between 1 to 30 per second, being 13 on average, and are usually quite regular. Increase in conditions of muscle warming. The cause is a decreased resting membrane potential in the denervated muscle.
- Fasciculations: long wave movements, crawling under the skin, very visible palpitations of the muscles. They are a spontaneous discharge of an axon causing contraction of muscle fibers in rippling unit and produce visible rippling of muscle. May originate anywhere along the course of the axon. In floxed persons they are a consequence of the motor neuron injuries caused by the toxicity of the quinolones. Once again, they are exacerbated by caffeine (that floxed persons cannot metabolize) and some drugs like theophylline or lithium.
- Fasciculations: short wave movements, a sort of buzzing of the flesh, perceived by the victim, but not easily visible. They are identical to the long wave fasciculations, but with a lower amplitude.

Twitching is a muscle reaction to abnormal nerve firings. There is a type of benign fasciculations but in floxed persons it is a symptom of neurological damage. In many floxed persons it starts in the eyelids and hands, but it is very common to have them in arms and legs. It is accompanied by a certain degree of weakness with no true prominent atrophy, especially in arms and legs. Areas plagued with fasciculations have normal sensory feelings. Fasciculations move from one part of the body to another and some days have a long wave amplitude and other days a short wave one. Normally the fasciculations are asymmetric at any given time. Some electromiograms of floxed persons have shown discreet signs of demyelination—without conduction blocks. The

fasciculations become chronic for months or years. Not more than two of the 42 floxed persons studied have had in common any serum antibody consistently elevated or abnormal. In fact, 97% overall of the serum analysis and antibodies in those subjects have not shown any abnormality, and those out of range readings have revealed a return to normalcy in further tests.

Many times, twitching is also accompanied by muscular cramps, especially in the gastrocnemius and other areas. Cramps are sometimes induced by exercise or touching the muscle and they can spread along the transverse direction across the muscle. Tendon reflexes are normal. Twitching does not usually develop in mild reactions. It is a typical symptom of intermediate and severe reactions. It starts any time from during the treatment up to several months later.

Fasciculations and/or cramps are early symptoms of myasthenia gravis, or amiotrophic lateral sclerosis, for instance. That is why these symptoms are so distressing especially when they last for years on end and are always ever present in daily life. Many severe floxies that take magnesium feel their fasculations increase, as well as their muscular pains (interestingly enough, magnesium is a well known counterindication in myasthenia gravis and other muscular autoimmune disorders). Again, in all these cases, serum CK may be mildly elevated. Six biopsies performed on five floxed persons have all shown lost of small caliber end-axons and less density of nerve endings. None of these floxed persons tested positive for antibodies to skeletal muscle, nor did the biopsies show any inflammation or lymphocytic proliferation.

PART VII: EXTENSIVE DAMAGE

32. TOXICITY GUARANTEED

Apparently there are not many studies of clinical significance that provide a wide explanation regarding the high toxicity level of quinolones. One can find medical reports suggesting that everyone having a bad reaction to fluoroquinolones had a previously underlying muscular disorder. We do not favor that theory. Also, there is no validity to the claim that all people having a reaction to quinolones have a common flaw or genetic component that make them more prone to suffer adverse events. The medical community will start to understand something about fluoroquinolones when they acknowledge that these antibiotics are just plain toxic.

Many of us have apparently not had an adverse reaction to the first three, four, ten or even twenty courses of quinolones over several years, but later on symptoms indicative of an adverse reaction culminate to the point where the patient is completely intoxicated from the quinolone. Many, many young, healthy and athletic patients just change in a short period of time from being the idyllic human model for every drug manufacturer, to becoming pharmaceutically intoxicated for many years or life, and then are labelled as psychotic, a hypochondriac, or diagnosed with serious neuropathies and pains that "were just lying dormant".

That is simply not true. The fluoroquinolones are toxic from the first milligram. Some people have livers that can metabolize more quantities of drug or body tissues that are more resistant than others, but everybody becomes intoxicated. Each person has different potential thresholds of resistance to the damage caused by quinolones:

LOWER THRESHOLD

Has been exposed above. It is delineated by strange bouts of tendinitis, abnormally long recoveries after exercise, less sleep and poorer quality sleep, some small throbbing pains in different parts of the body, occasional twitching, feeling some stiffness, decreased tolerance to coffee, loss of memory, especially short-term.

UPPER THRESHOLD

The symptoms that you have experienced are those corresponding to the severe reactions, intermediate reactions and mild reactions. It is too late to expect a rapid resolution, and according to the level of the intoxication- long, hard and miserable times may lay ahead.

The toxicity of quinolones acts in two preferential ways:

- direct chemical destruction (cartilage, cellular functions and organs).
- mild, long-lasting or irreversible vasculitis, with neuropathic after effects.

Obviously, you will not find many doctors willing to admit these two phenomena do actually occur. But the sooner more research is conducted in that direction, the further we will advance in terms of understanding the problem.

The following section of the report deals with some of the most important problems caused by quinolones.

33. IMPAIRED HEALING IN THE FLOXED BODIES

This is another very distinct characteristic of quinolone disorders, of which every doctor is unaware. Once you become asymptomatic because you have been taking care of yourself and restraining from exertional activities, you might well think that your ankle is nearly recovered from an intermediate reaction (say in grade G2 according to table 9 at the end of the report). But if not enough time has elapsed since the ingestion of the drug (less than 2 years) then only a number of repetitions of an exercise with your foot against strong resistance can bring you again to Grade 9 (see same table 9). So, returning to normal pre-floxed levels of activity is not indicated by a lack of symptoms but by a continuously probing (trial and error) method, not without relapses and danger.

The floxed body has been depleted of nearly all of its natural healing capacity. To function properly, the body must continuously produce new tissue, especially cellular matrix, collagen and fibrous cells. For everybody, the toxicity of the quinolones kills these mechanisms, in a dose dependent manner.

So whenever you accidentally bump a part of your body, especially the hand or foot (more distant areas and less irrigated tissues) it takes an abnormal amount of time to recover. Small blows that in a normal situation would take three days to heal, can take up

to three months of healing during the acute phases. A cut in the skin around the Achilles will take the same time to heal as in any other area of the body, but ten to twenty times longer for the scar to clear off.

When the athlete approaches grades 6, 7, 8 and 9 (table 9), there is a lot of deposition of waste in the joints and under the skin. That causes the waste to adhere to the joints and worsen the symptoms. Massage helps to remove those deposits in most cases.

During the months that follow the acute phase, both mechanisms (healing and rebuilding) are slowly returning to normal, especially the quality of the rebuilding, although the healing response still cannot keep up with the requirements of our previous (pre-floxed) level of activity. There are many scientific reports that show ciprofloxacin impairs the healing of broken bones and connective tissue. Being floxed is not the best time to undertake minor surgery that could be avoided or rescheduled for later.

So, during the acute phase it is not possible to cope with strenuous or very repetitive activities. It is normally advised to maintain some degree of physical activity, but always testing and probing the limits, without surpassing them.

Quinolones make it more difficult for people to recover after exercise, and can cause them to develop a frank intolerance or dislike to exercise. Pains and stiffness after exercise are very characteristic of this toxicity. That is most likely due to a chemical damage of the fascia (connective tissue) that exists between muscles and allows them to run smoothly and independently. These lesions can last for many years after the floxing.

34. AVOID ANY PHYSICAL TRAUMA

It has been previously elucidated how a normal strain on a floxed person can have more serious consequences than on a normal person. In severe reactions, small blows or edemas can cause a flare up of minor neurological problems all over the body in less than two hours; for example, twitching, lack of jaw coordination, tremors, as well as local alterations much more intense than usual.

Severe impacts or traumas directed against a limb (a quad or a calf for instance) can be devastating for a floxed person. The inflammatory process in the area will affect the main nerves and trigger a neuritis that can take several years to resolve. So, an injury that in normal conditions would take up to 1 to 3 months to heal can be a long-term threat, or become a chronically impairing condition for a floxed person. This provides another clue for investigators because it is clear that there is a link between the processes of inflammation and the exacerbation of the floxing conditions. After the traumatic event, there is a release of mediators in the bloodstream that induce alterations of the vessels all over the body and also promote the arrival of immuno-complexes to the site of the injury. Some of these compounds and mechanisms could be of the same type as the ones that cause the damage induced by the chemical toxicity of quinolones.

For the examples cited, in the case of a blow or strike to a quad, the neuritis can affect the whole upper leg, from buttock to knee, providing strong, stabbing neurological pains to the sufferer. A traumatic event in the calf can initiate a neurological response in the outer (lateral) knee, and in the Achilles tendon.

PART VIII: MUSCULAR PAINS

35. PAIN LEVELS

Pain levels experienced throughout the floxing can range from very low to the maximum on a 10-point scale. Pains of the maximum severity: stabbing, jabbing, tearing, and ripping, can be felt when a joint or limb collapses neurologically. These pains are described as higher than passing a kidney stone or rupturing a testicle, for instance, and can completely block the affected joint. Intermediate pains are common with mono-neuritis in legs, arms and neck, especially at night and with some minor movements. Low intensity pains (that correspond to myalgias) typically spread all over and correspond to the "normal" state of a floxed person: just feeling like a person that is 40 years older than their current age. See later for more information on neurological pains, how they can affect daily life and how little can be done to palliate them.

36. CONSTANT PAIN ALL OVER. MYALGIAS

Besides the neurological pains, in severe reactions, constant, intense and body-wide pains are very common. Basically they are drug-induced myopathies, again probably secondary to the vasculitic reaction. The major symptoms in drug-induced myopathies are proximal muscle weakness (quads, hamstrings, shoulder, biceps, triceps), slightly increased muscle enzyme levels (although sometimes can be normal), electromyographic changes and histological lesions. Quinolones induce painful myopathies associated with neuropathies that could be called painful neuro-myopathies. According to the established medical research, typical of these neuro-myopathies is a free period between the beginning of the treatment and the appearance of symptoms, and incomplete resolution after withdrawal of the treatment.

In fact, myopathy is defined as any abnormal condition or disease of the muscle tissues, commonly involving skeletal tissue. Many drugs have been implicated as causes of myopathy, although quinolones are frequently left out by medical manuals, normally because each manual copies from other previous fact sheets and there is little new research behind new editions. The widespread myopathies caused by the quinolones are another "*postmarketing anecdotal finding*" according to laboratories, and are not still regarded as a common source of muscular pain.

Quinolone myopathy, like other drug-induced myopathies, usually develops insidiously. The onset of clinical manifestations can occur days to months after exposure to the causative agent, according to Zuckner and Mastaglia (see references). Commonly, patients present with non-specific complaints of progressive, generalized muscle weakness, muscle pain (myalgia) or fatigue. Severe reactions to quinolone antibiotics (prolonged courses or high doses) present with severe myalgias and debilitating weakness, especially in proximal muscles (quads, hamstrings, upper arms) that leave many floxed people completely crippled, bedridden or in a wheelchair for months.

Drugs may cause muscle injury by direct, indirect, or immunologically mediate mechanisms. Again, we do not know the exact mechanism of injury behind the quinolones but it might be a drug-induced immunological action directed at the muscle, already mentioned as immune complex-mediated myositis. It is a type of inflammatory myositis and that is the reason why floxings resemble other inflammatory illnesses so much.

Nevertheless, we do not have the means to discover the mechanism of the lesions, and the medical class is not devoting enough research to find an answer. As a consequence only a guess can be attempted. Quinolone myopathies could have a direct myotoxicity, as the toxicity exhibited by the statins (used to treat high cholesterol), associated with vacuolar myopathy, or other common drugs that cause mitochondrial myopathy, which symptoms also resemble very much a floxing reaction.

The muscular pain caused by quinolones is defined by some doctors that have treated difficult cases of quinolone toxicity as a sort of "*low grade*" myoglobinuria-rhabdomyolysis. These illnesses, when fully developed, are very dangerous, and have a fatal potential. There are many reports of fulminated deaths caused by quinolones due to both of these mechanisms. But in general, for floxed persons, they tend to show a more manageable profile, although very damaging.

Severe reactions typically show a slight elevation of the serum myoglobin levels that can also stay at the upper normal range for some 4 years. For the same length of time the CPK enzyme (creatinephosphokinase) may be elevated—normally on the hundreds, or low thousands figures.

The cause of both alterations probably is muscular necrosis caused by the quinolone induced vasculitis. Symptoms are very well known for long term floxies: generalized pain, decreased range of motion, stiffness, soreness; and all of the symptoms increase

with activity.

The pathology exhibited by the floxed persons is necrosis of muscle fibers with a releasing of muscle components into circulation. The doctors consulted think that muscles are injured due to both:

- a rise in free intracellular calcium due to damage to muscle sarcolemma and a failure of energy supply within muscle cell.
- an activation of calcium-dependent neutral proteases & phospholipases that destroys myofibrillar, cytoskeletal, and membrane proteins and the ensuing lysosomal digestion of muscle fiber contents.

Typically, the severely affected floxed person exhibits clinical features of muscle involvement (weakness, stronger proximal, rather than distal; discomfort in terms of pain and tenderness; swelling). There are also many case reports of renal injuries, (acute interstitial nephritis, renal impairment, proteinuria (i.e foamy urine), and extremely severe rhabdomyolysis that can be fatal, accompanied by a dark urine that is tea colored). A good deal of floxed persons also have a fever for some months when the crisis is more acute.

As explained before, many sedentary floxed persons believe that they are healed two years earlier on average, than when they are actually cured, because the symptoms of small neuromuscular damage do not become evident unless the patient performs some type of physically demanding activity.

The main determining factors for neuromuscular pains in affected floxed persons are: increased age, exercise, fasting, hypokalemia (low potassium levels).

The main tests to be performed in order to assess the renal involvement of the muscular destruction are:

- Hyperkalemia (high potassium levels). High levels are caused by muscle breakdown and also by renal failure.
- Hypokalemia (low potassium levels). Causes myoglobinuria. Also painless proximal weakness.
- Hypercalcemia (high calcium levels): Due to release from muscle and possible reduced renal excretion.
- Hypocalcemia (low calcium levels): Due to binding by damaged muscle & hyperphosphatemia (high phosphorus levels)
- Hyperphosphatemia & Tissue calcification : Due to release of organic & inorganic phosphates from muscle.
- Test also for serum (blood) levels of myoglobin (high levels in muscular destruction and renal compromise, may be caused by quinolonic ischemic vascular occlusion), hemoglobin, CPK (muscular, heart and brain destruction), lactate (see below), carnitine (if low the quinolones have affected the β -oxidation process)
- Test also for urine levels of myoglobin, albumin and hematuria
- Special meaning of the test for serum lactate: There is no increase with exercise in glycogenoses (disorders of the glycogen storage); but there is a rise with minimal exercise when the quinolones have induced a mitochondrial disorder.
- The ultimate test is a muscle biopsy usually showing destruction of small nerves, plus scattered muscle fiber necrosis and degeneration.

The quinolone family specifically may cause:

- glycogen metabolic disorders, especially those altering the aldolase, lactate dehydrogenase, phosphoglycerate kinase and phosphorylase kinase.
- fatty acid oxidation disorders
- mitochondrial disorders, the most common through a deficiency in coenzyme Q10.

The coenzyme Q10 (also called ubiquinone) deficiency deserves a special consideration. Clinically it manifests as exertional fatigue, high myoglobinuria (precipitated by fever, and mild to moderate exercise), proximal weakness (quads, hamstrings, biceps, triceps) and afflictions to the central nervous system (mainly cognitive impairment). On a biopsy, muscles can show ragged red fibers with prominent lipid accumulation.

Some floxies also have all the symptoms of a neuroleptic muscular disorder. The symptoms are muscle rigidity, dysarthria, dysphagia, hyperthermia (fever), tachycardia, incontinence, tachypnea, hyperhidrosis (excessive sweating), all of which usually resolve during the first stages of the recovery process.

PART IX: SPECIFIC LESIONS

The quinolones cause many lesions in the whole body. More evident are those inflicted to the intestines, kidneys, liver, pancreas, heart and brain.

In this section, there are some references to them. For a quite exhaustive relation of medical reports of quinolone damages on all organs, visit www.fqresearch.org.

37. CENTRAL NERVOUS SYSTEM EFFECTS

Although much about the pathophysiology of fluoroquinolone-related CENTRAL NERVOUS SYSTEM effects remains ill-defined, one hypothesis suggests that drug interactions with the g-aminobutyric acid receptor (GABA), an inhibitory neurotransmitter, may explain CENTRAL NERVOUS SYSTEM-stimulating effects. Ciprofloxacin, enoxacin, and norfloxacin demonstrate high-affinity binding to GABA_A and interfere with GABA binding to its receptor. (See next chapters for an understanding of the role of GABA nerve receptors)

Furthermore, some NSAIDs (non steroid antiinflammatory drugs) have been shown to enhance binding of fluoroquinolones to GABA receptors. Coadministration of fenbufen and a fluoroquinolone can induce convulsive seizures.

Fluoroquinolones can also induce excitatory effects through direct activation of N-methyl-D-aspartate (NMDA) and adenosine-receptor mechanisms. Thus, it may be that it is only under specific conditions of sufficient CENTRAL NERVOUS SYSTEM penetration, coupled with threshold antagonism of inhibitory pathways (GABA) and stimulation of excitatory pathways (NMDA, adenosine), that observable CENTRAL NERVOUS SYSTEM symptoms are manifested.

38. VISION ISSUES

It has already stated that vision damage is so disturbing and debilitating that just on the grounds of vision lesions, quinolones should be restricted only for special high-risk therapies.

Floaters: The mechanism of damage may be a toxic-vascular lesion that in turn may cause a small amount of bleeding inside the eye, which may appear as a group of floaters. They could also be caused by crystal-like deposits that form in the vitreous, and we have not still gathered a conclusive causative factor. Floaters may sometimes interfere with clear vision, often when one is reading. If a floater appears directly in your line of vision, moving your eye around will cause the vitreous to swirl around and will move the floater out of the way. Looking up and down rather than back and forth will cause different currents inside the eye and may be more effective in getting the floater out of the way. Floaters tend to be a permanent lesion in severe reactions. They lose intensity with time but it is really improbable that they disappear spontaneously.

Flashes: Flashing lights is the sensation of lights going on and off, noticed particularly off to one side. They tend to occur in only one eye at a time and persist even when the eye is closed. Some doctors hold the opinion that the flashes are caused when the vitreous, a clear gel-like substance that fills the inside of the eye, sometimes pulls or tugs on the retina. This pulling causes the appearance of flashing lights or lightning streaks, though there is no flashing light actually present. Given the toxic mechanism of all the disorders of the floxed persons, other doctors believe that the flashes are generated in the brain, caused by a spasm of blood vessels, what they call ophthalmic migraines, normally with a little or no headache but possible eye pain. These lights last many years in severe reactions and are very sensitive to foods and supplements, for instance soy and sugar provoke a massive proliferation of them.

Macular degeneration: At the back of the eye there is a thin layer of light-sensitive nerve cells and fibres called the retina. We see things because light entering the eye strikes the retina and is turned into an electric impulse that the brain understands as an image.

Near the centre of the retina is a small spot about the size of a pea called the macula. The macula processes the details in the central part of the image that the brain receives. The macula needs good light to work efficiently and works best in daylight. The rest of the retina is responsible for side, or peripheral, vision. It is especially sensitive to dim light, which makes night vision possible. If the macula deteriorates for some reason, the retina becomes like a

camera with a spot on the film. The centre of the field of vision blurs and all detail is lost. This condition is called macular degeneration. Quinolones tend to damage the retinal blood vessels that supply the macula. In severe reactions, cut off from its source of nourishment, the macula is permanently damaged and some blurry central spots appear in one or both eyes. Ophthalmologists can diagnose these lesions, that are not accompanied by depigmentation.

Dry eye: Explained in other sections of the article. Can be very limiting also. Commonly appears some months after exposure and symptoms start to alleviate after year 3 in severe reactions. Very often floxed persons that are not aware of their reaction are diagnosed as having Sjögren's syndrome.

Curtains: These are very long-lasting lesions of the visual field usually called curtains. They can be seen in the upper part of the vision field and move horizontally around bright fluorescent lights and brilliant backgrounds. They are like a string of water drops moving like a curtain from side to side of the upper part of the vision field.

Eye pain: Eye pressure and pain is typical. Sometimes eye pressure comes in wave-like bursts. It resolves earlier than the rest of vision issues. There is also a marked loss of strength on the muscles that move the eye and especially those that bend the cornea, making it very difficult for the eyes to focus. By year 2 cornea control starts to resolve and by year 3 the rest of the muscles of the eye begin to recover, so the floxed person feels clearly that he regains strength in the muscles of the eyes.

Complete loss of vision: Some floxed persons, very severely affected, have lost their vision completely up to 4 times. The loss of vision comes suddenly, and in a matter of seconds the floxed person can see only a solid blank field. It can last from 30 seconds to 6 minutes. This phenomena is described in the medical literature for ciprofloxacin.

Phototoxicity: Two types of photosensitivity reactions have been associated with fluoroquinolone therapy: photoallergic reactions and phototoxic responses. Photoallergic reactions normally require previous exposure to a drug in the class. In contrast, phototoxic responses are more common and can develop without previous exposure to a fluoroquinolone if the dose of the photo-labile drug and exposure to UVA light (around 350 to 360 nm) are sufficiently high. Photosensitivity reactions are postulated to occur as a result of fluoroquinolone photodegradation, as well as the molecule's ability to generate free monovalent oxygen radicals. In turn, these oxidative radicals may attack cellular lipid membranes, initiating inflammatory processes, and eventually produce DNA damage. Evidence for photo-induced oxidative DNA damage is demonstrated by the development of murine tumors in mice treated with lomefloxacin.

Be aware that there are many ophthalmic preparations based on quinolones, especially cipro. If you have suffered a small reaction to any quinolone before, these medications can cause permanent damage to your vision. Some new formulations have been released for the pediatric population (older than 6 months) with a mixture of cipro and a cortico-steroid.

Some floxies have lost their vision completely for some minutes several times after taking the antibiotic. It is a scaring experience, that can have a dramatic end:

Deaf and blind due to the ingestion of a fluoroquinolone 2002. Canadian Adverse Reaction Newsletter Volume 12 · Issue 4 · October 2002. Case Presentation - moxifloxacin (Avelox):
Optic neuritis developed in a 22-year-old woman with sinusitis while she was receiving moxifloxacin (Avelox) therapy. After 1 dose she experienced fainting and somnolence, which resolved 2 days after initiation of therapy. After 4 days of treatment she lost vision in her left eye. She consulted an ophthalmologist and continued therapy for 6 days. An MRI scan ruled out multiple sclerosis. The patient was taking birth control pills concomitantly. It was reported that her vision would not likely return.
Ciprofloxacin: suspected association with deafness and reduced hearing Health Canada has received 4 serious case reports of deafness or decreased hearing suspected to be associated with ciprofloxacin. They involved men aged 35, 47, 65 and 67 years old. Three were receiving 1000 mg/d orally and one was receiving 800 mg intravenously. In all cases, the reactions began within 1 week after initiation of therapy. Three patients recovered, and the fourth experienced partial permanent deafness.

39. QUINOLONES AND DAMAGE TO THE HEART

[in preparation]

This is probably the quinolone disorder that kills more people. Many people develop heart beat irregularities that can be very life menacing.

Re-exposure to quinolones cause the heart irregularities to return with an increased severity, according to the experience of all the floxies that suffered repetitive intoxications. Strong abnormalities with the heart last typically for some 2,5 years after a severe intoxication, and 1,5 years for intermediate intoxications with quinolones.

Heart pathologies caused by quinolones are one of the most under-reported ones. People visit their doctors complaining about

their hearts and none of them ask them about the medications they have taken in the past months, and we don't know of any case in which the cardiologist has asked about antibiotics taken in the past.

There have been many reports of cardiovascular effects, particularly prolongation of the QT interval corrected for heart rate (QTc interval), with quinolone therapy. This finding may relate to the incidence of severe cardiac events that resulted in the withdrawal of grepafloxacin. Furthermore, the manufacturer of sparfloxacin recommends that the drug not be administered to patients with known QTc interval prolongation or to patients receiving concomitant pharmacotherapy that might increase the interval, induce bradycardia, or promote torsades de pointes (eg, class Ia and III antiarrhythmic agents, bepridil, cisapride, erythromycin, or tricyclic antidepressants).

It appears that this effect may be more predictable with medications coadministered with quinolones that inhibit cytochrome P-450-mediated metabolism because of increased drug accumulation. Different quinolones differ in the structural modification of the precursor nalidixic acid. It seems that no specific structural modification has been associated with cardiovascular effects, including those that might influence cytochrome P-450-mediated metabolism, so it is a class effect. No structural modification has been associated with the increased incidence of serious cardiovascular events associated with grepafloxacin therapy, although clinical studies did show associated QTc prolongation. Grepafloxacin, which was introduced in August 1997, was voluntarily withdrawn from use in October 1999 because of reports of severe cardiovascular events among patients taking the drug.

Some floxies have required the implantation of pacemakers to have their heart beats regularized.

40. QUINOLONES AND GENETIC TOXICITY

Quinolones have been shown to inhibit mammalian cellular topoisomerase II, which correlates with in vitro cytotoxicity in those cells. Some quinolones have an increased potential for cytotoxicity, with the effect being additive. However, disruption of the chromosome, or clastogenicity, usually occurs only at very high drug concentrations, and surveillance studies following clinical introduction of the drugs have not found any carcinogenic potential linked to fluoroquinolone use.

41. QUINOLONES AND DAMAGE TO THE DIGESTIVE SYSTEM

[in preparation]

42. QUINOLONES AND DAMAGE TO THE KIDNEYS

[in preparation]

Quinolones, and especially ciprofloxacin, are linked clearly with acute renal failure. They should be prescribed carefully to patients with impaired renal function. Quinolones can destroy some of the microtubules of the kidney that filter the blood. Once again it seems that it is due to a vasculitic ischemia (narrowing of the micro-vessels of the kidney) that induces a necrosis of critically important glomeruli and tubuli in the kidney. This condition leads to progressive kidney failure, an end-stage condition that requires either hemodialysis or a transplant. The only symptom that causes a first stage kidney damage can be foamy urine.

43. QUINOLONES AND DAMAGE TO THE PANCREAS

[in preparation]

Quinolones are very toxic drugs for the liver, pancreas and kidneys. It is typical to have elevated liver and pancreas enzymes counts for months or years after the treatment.

44. QUINOLONES AND DAMAGE TO THE LIVER

The pathophysiology of adverse hepatic events and hypoglycemia caused by quinolones remains unknown. All quinolones are toxic for the liver, specially for large treatment and/or dosage, as explained earlier. The most serious toxic effects have developed with the use of three agents: temafloxacin, trovafloxacin, and grepafloxacin. The "temafloxacin syndrome" was characterized by hemolytic anemia, renal impairment, hepatotoxicity, disseminated intravascular coagulation, and hypoglycemia. Acute renal failure developed in nearly two thirds of the patients with temafloxacin syndrome.

In addition, mild hepatobiliary changes were observed in half of the patients and coagulopathy in one third. The development of these adverse drug reactions resulted in the withdrawal of temafloxacin from the market in 1992,

Quinolones, especially when taken in large doses or for extended periods of time, are toxic to the liver. It seems that the most common injuring action is cholestatic damage. Cholestatic means a reduction of the bile flow, due to reduction of the secretions or obstruction of the biliary tree. The damage manifests as hepato-cellular damage.

Quinolones cause elevations of liver enzymes that return to normal in most of the cases after several months, but that can be persistent in severe reactions. Bilirubin is usually elevated, indicating some sort of necrosis.

The worst common effect on the liver is the impairment of the P450 pathway, what causes:

- inability to metabolize many other drugs that you may need to take in the future
- inability to metabolize coffee
- inability to metabolize more quinolones, so new treatments can reach rapidly toxic doses

45. QUINOLONES AND THE LIVER P450 ENZYME PATHWAY

The liver produces a compound of enzymes that metabolize (through a two phase degradation) most of the toxic substances and drugs that enter the body. The most important group of those enzymes is called the P450 set.

Quinolones are powerful inhibitors of some of the P450 enzymes, primarily the P450-1A2 and the P450-3D4. But these two enzymes are needed to metabolize other substances that may enter your body. If your liver enzymes are still inhibited (not active in enough quantities) by the action of the quinolones, the concentration of the new substances that enter your body can reach toxic levels. For instance, if your P450-1A2 enzyme is largely inhibited after you have ingested cipro or levaquin, and then you drink a cup of espresso coffee, the caffeine concentration in your body can be 6 to 10- fold higher than in normal situations, bringing you to the edge in terms of nervousness and agitation.

With other drugs the same effect can have serious consequences because some other drugs are very toxic in high doses.

The inhibition of the P450 enzymes by the quinolones helps explain many facts that floxed persons experience, for instance:

-Some foods, chemicals and medications for pain or inflammation control have different consequences in floxed persons, depending largely on the level of normalcy of the P450 enzymes that tend to be inhibited by quinolones.

-Recovery takes much longer for people with strong inhibition of enzymes caused by the quinolones. The inhibition of the P450 enzymes caused by quinolones is usually regarded as reversible, but some evidences point to long term, or semi-irreversible inhibitions.

-Perhaps, the different type of metabolization capacities of people is the most idiosyncratic aspect of a quinolone reaction.

There are some commercial tests available that can assess the status of the main P450 enzymes. A way of checking how your liver is returning to normal availability of P450-1A2 enzymes is to take some caffeine from time to time and check whether the effect is far from or the same as before the floxing. In severe floxings, returning to normal levels of P450-1A2 enough to metabolize coffee properly, can take 5 years or more. In mild floxings, the sufferer can resume drinking coffee after a few months.

Curiously enough, smokers could have a slight protection against inhibition of the P450 enzymes caused by quinolones, because smoking promotes (activates) the P450-1A2 production.

In the case of quinolones, once again, the evidence of dose-dependent inhibition of P450 is consistent with a number of recent studies suggesting the determination of in vivo inhibition constants based on plasma concentration of inhibitor, the higher the doses, the greater the inhibition.

All the quinolones more or less suppress the same enzymes, but for ciprofloxacin, probably the most extensively studied quinolone in regard to this aspect, it significantly suppresses gene expression of P450-1A2, P450-3D4, P450-2C11 and P450-3A1.

Ciprofloxacin is a quinolone antibiotic and a potent competitive inhibitor of CYP1A2. Ciprofloxacin is metabolised up to 75% and partially excreted, unchanged in the urine. In many trials the inhibitory potency of ciprofloxacin caused a 70% reduction in the CYP 1A2-mediated demethylation rate of caffeine in vitro. Furthermore, the activity of CYP3A4 was decreased by 65% in human hepatic microsomes by ciprofloxacin.

As said before, medications are often metabolized by enzymes in the liver so that the medication can be more effectively removed from the body. The biggest mistake that the medical class is making again is considering that the inhibition of the enzymes caused by quinolones takes place as long as the drug is ingested. Doctors and researchers believe (because they have not investigated counterwise) that activation of P450 enzymes return to normal once the quinolone is discontinued.

That is a big mistake with serious consequences. After a floxing, the P450 inhibition can last for months or years, depending on the severity of the fluoroquinolone toxicity. Thus, there can be a "virtual interaction" between the quinolone and a new drug that a floxed person takes one year after being floxed. This can be difficult for your doctors to understand because they think that the quinolone is no longer in your body, and perhaps they are right, but crudely true as the effect on the P450 pathway is still present.

So, floxed persons can exhibit signs of drug "interactions" with his/her formerly taken quinolone when the liver damage interferes with the removal of another medication. For instance, ciprofloxacin taken in the past after a strong reaction, can inhibit (prevent the activity of) one of the pathways that is used to eliminate medications from the body some years later. Some of the medications that use CYP1A2 for an elimination pathway are listed below. If CYP1A2 (another way of naming P450-1A2) is inhibited, and the dose of these medications is not reduced, the medicine could accumulate in the body to levels that could cause serious adverse drug reactions.

In addition to inhibiting drug metabolism, ciprofloxacin could be involved in other types of drug interactions. Since ciprofloxacin can have adverse effects in the brain, including seizures, it should be used cautiously with other drugs that can have similar effects.

For instance, drugs that can reach toxic levels after a former reaction to ciprofloxacin are:

1A2: acetaminophen (paracetamol), amitriptyline (elavil), diazepam, caffeine, chlordiazepoxide, clomipramine, clopidogrel, clozapine, cyclobenzaprine, desipramine, estradiol, flutamide, fluvoxamine, haloperidol, imipramine, mexiletine, mirtazapine, naproxen, nortriptyline, olanzapine, ondansetron, phenacetin, propafenone, propranolol, riluzole, ropivacaine, tacrine, theophylline, verapamil, warfarin, zileuton, zolmitriptan.

3D4: alfentanil, almotriptan, alprazolam, amitriptyline, amiodarone, amlodipine, amprenavir, aprepitant, astemizole, atorvastatin, bepridil, bexarotene, bromocriptine, budesonide, buprenorphine, buspirone, busulfan, cafergot, cannabinoids, caffeine, carbamazepine, cerivastatin, cevimeline, chlorpheniramine, cilostazol, cisapride, citalopram, clarithromycin, clindamycin, clomipramine, clonazepam, clopidogrel, cocaine, codeine, cyclobenzaprine, cyclophosphamide, cyclosporine, dapsone, delavirdine, desogestrel, dexamethasone, dextromethorphan, diazepam, dihydroergotamine, diltiazem, disopyramide, docetaxel, dofetilide, dolasetron, domperidone, donepezil, doxorubicin, dronabinol, dutasteride, efavirenz, eplerenone, ergotamine, erythromycin-(not, 3A5), esomeprazole, estrogens, estradiol, ethosuximide, etonogestrel, etoposide, exemestane, felodipine, fentanyl, fexofenadine, finasteride, flutamide, fluticasone, fluvestrant, galantamine, gleevec, haloperidol, hydrocodone, hydrocortisone, ifosfamide, imatinib, imipramine, indinavir, irinotecan, irradipine, itraconazole, ketoconazole, LAAM, lansoprazole, lercanidipine, letrozole, lidocaine, lopinavir, loratadine, losartan, lovastatin, methadone, methylprednisolone, miconazole, midazolam, mifepristone, mirtazapine, modafinil, mometasone, montelukast, nateglinide, nefazodone, nelfinavir, nevirapine, nifedipine, nifedipine, nimodipine, nisoldipine, nitrendipine, norethindrone, omeprazole, ondanestron,, oral, contraceptives,, oxybutynin, paclitaxel, pantoprazole, pimozone, pioglitazone, prednisolone, prednisone, progesterone, propranolol, quetiapine, quinine, quinidine-(not, 3A5), rabeprazole, repaglinide, rifabutin, rifampin, ritonavir, salmeterol, saquinavir, sertraline, sildenafil, sildenafil, simvastatin, sirolimus, tacrolimus, tamoxifen, taxol, telithromycin, temazepam, terfenidine, testosterone, tiagabine, tolterodine, toremifene, tramadol, trazodone, triazolam, trimetrexate, valdecoxib, verapamil, vinblastine, vincristine, vinorelbine, voriconazole, R-warfarin, zaleplon, zileuton, ziprasidone, zolpidem, zonisamide.

The floxed person only has reason to worry if his/her reaction has been severe. For mild and intermediate reactions, the inhibition of the P540 pathways returns to normal in some month's time. Do not make any decision on your own, always consult your doctor and do as you agree with him. If you have to take any of the above listed drugs for an extended time, suggest to him to test you prior to and during the treatment, to detect possible overdosing effects.

Differences in individual availability of P450 enzymes might very well be behind many susceptibilities to quinolone treatments because these enzymes play an important role in chemical sensitivity. Thus, those with a mutation of CYP1A2 could detoxify cipro at only 0.5%-20% of the normal capacity, resulting in acute hypersensitivities (not allergies) after a single pill.

It is well known that in the Korean War, soldiers with G6PD deficiency were hypersensitive to an anti-malarial drug. Among people there is a 40-fold variation in P450 1A2, the most important of the P450 enzymes necessary to detoxify quinolones and chemical substances. Many subjects suffering from multiple chemical sensitivity are now known to be P450-compromised. It seems possible that different reactions to quinolones can also be modulated by P450 availability. It also looks plausible that repetitive treatments with quinolones can impair the P450 pathway even for people that initially had a large metabolic capacity, so the patients tend to become more and more sensitive to quinolones with successive treatments.

46. OTHER DISORDERS YOU MIGHT EXPERIENCE

Half of the quinolones marketed since their creation have been withdrawn from the market because of their potentially fatal toxic profile. Some had a marked inclination to destroy the liver (trovafloxacin), others the heart, and all are very toxic to vital organs as a class effect. It is not uncommon to get abnormal results in serum tests for many months after discontinuation of the drug.

On top of the general problems that you may have due to the toxicity of the quinolones, many people have additional problems, due to alterations of functions or systems that were working well but in delicate equilibrium before taking the quinolones. For instance, if without knowing it you suffered a little osteoarthritis because of overuse during your endurance sports, or a short leg, asymmetrical muscle mass, lack of flexibility or the like, all of them will become very noticeable when your floxed body cannot compensate for any minor flaw.

When you suffer strong quinolone-induced neuropathies of the extremities, you will experience a great loss of function and some atrophy (wasting) of the main muscles. Sometimes it is very difficult to detect unless tested by a professional. But you can notice that your legs can hardly raise you up, or are nor longer able to climb stairs by the many. Muscles most frequently subject to

wasting are the tibialis anterior, soleus, gastrocnemius, vastus medialis, the other quadriceps muscles, and the shoulder and forearm muscles.

Atrophy of the muscles that control a joint make this joint more prone to injury, normally from repetitive loads. So the vicious cycle starts: the neurological lesions waste the muscles, so joints are overloaded, or eccentrically or abnormally loaded, and they degrade, creating another layer of pains and disability that combines with the previous one and that contribute to a never ending "snowball effect" injury.

So, it is important that as soon as you feel well enough that you begin a stretching (mild to avoid neurological irritation) and strengthening (mild to avoid cartilage degradation) training program for your most affected joints.

The neuropathies caused by fluoroquinolones also affect the nerves that control the chest muscles, so the floxed person tends to breath abnormally, and with very shallow chest movements. As a result, not enough oxygen is introduced in the system, and some metabolic processes become even more impaired. Insomnia is greatly worsened by shallow breathing.

47. MIXED CONDITIONS

This report does not deal with a floxing in context with other previously existing health conditions. Floxing is a very debilitating illness in and of itself, but its complications can multiply if before the drug intoxication there were other pre-existing disorders such as lupus, lyme disease, rheumatoid arthritis, multiple sclerosis or even osteoarthritis.

PART X: CAN THIS REALLY BE HAPPENING TO ME?

48. THE PSYCHOLOGICAL ASPECT IN SEVERE REACTIONS

You were a young active person, lead a healthy life, and ate healthy. You had a good job and were a brilliant professional. Your family is lovely. You merely had a minor health problem like a sinus infection, a sore throat, a urinary tract infection or a suspected or actual prostatitis. You trusted your medical system and you were prescribed a quinolone antibiotic. Finally, you have had a severe reaction.

Now you cannot play any sport, not even playful wrestling with your children. You have cognition problems that disrupt or stress your career. You can hardly sleep. Your vision is constantly bothering you, reminding you all day long that you are ill. You feel constant, intense and strange pains, you cannot sit in any comfortable position, you have problems getting in and out of the car, and you resemble an 80- year old man. You have to watch what you eat carefully, so you are barely able to attend social events anymore. For months on end your symptoms get worse by the day.

Some nights you cry in solitude. You have little understanding and/or compassion from your loved ones because you still look normal on the outside. It is 3 years since you got hit and your youngest child does not know what you were like before the floxing because he was too young; he only knows you as a permanently ill father that cannot even eat normally. Perhaps your co-workers think that you are exaggerating or pretending that you are ill. Your doctors are not willing to listen to you correlating your problems and symptoms to a fluoroquinolone antibiotic. After a year or so, your symptoms have gotten worse, but surprisingly all of your acquaintances, friends and relatives give up sympathizing with your situation because it is lasting so long, so you start to feel more alone. Many suggest, or tell you boldly, that your problems are all in your mind.

Most tests are negative so you remain undiagnosed. All severe cases reveal abnormalities in neurological studies but they are attributed to physical compressions for instance and they offer you a surgical release that you know won't fix anything. Nothing seems to help with your recovery. Nobody seems to have any knowledge about your disorders. You spend enormous sums of money and time on doctors and palliative therapies. Your daily life is a constant struggle against your illness, and you cannot release yourself from your daily obligations because nobody acknowledges your chemically altered state, and so you become stretched to the limit.

After the first stage, in which you just fight for mere physiological and psychological survival, one day you find yourself staring at people just getting out of the car, sitting in awkward positions, walking up stairs, walking normally, eating normal food in a good restaurant, planning to trek, bike, travel or play, and dream of a day in which you will also do it as effortless and so unaware of doing so as you did before the floxing.

Note:

Try to seek help from loved ones and caring doctors. You will need it.

You are going to need some help, either from a professional, your family, from friends or from support groups. But it is very difficult for a non-floxed person, even a loving and caring one, to truly grasp the magnitude of your chronic suffering from a quinolone antibiotic. This is not a matter of weeks or months, but of many years. After 2 or 3 years you cannot remember any longer how it was like to feel physically normal. You become increasingly weary and long for a normal life. You are scared about the permanent injuries you seem to be facing, and above all you do not know what lies ahead in terms of limitations and deterioration. Your mental drive sometimes falters and you are overwhelmed by the floxing in every way. Depression will linger. Suicidal thoughts are not uncommon, but in most cases, they are short lived or insufficiently based, although repetitive. Some floxed persons have taken their lives.

Be prepared for very distressing and disheartening states of mind and body and be determined to keep moving forward. Stay positive as much as possible. Time is your only real friend in this unequal and unfair fight. Mild and intermediate floxings usually have a happy end. After a severe floxing it is unlikely that you will recover your former self entirely. And after realizing it you will have to admit it and then reschedule your life because of it.

49. IT IS ALL IN YOUR HEAD

As a result of the intoxication, you may have actually suffered a mental damage. Those cases are not treated in this paper. We are

assuming that you have been lucky enough that your brain has withstood the treatment with the quinolones, so most likely, your mental status will have suffered but your mental integrity will be untouched save those initial alterations very common in the acute phase: depersonalization, crying episodes, panic attacks and the like.

On the other hand, if you have suffered a strong reaction and if you were healthy before, you know perfectly well what are your symptoms and you do not need help to identify them or to assess the limitations that they impose on your life. You might also be scared by the unknown evolution of your lesions, and be a little depressed by your overall current situation.

That sadness, that is humanly natural, will be perceived by many people that surrounds you and perhaps one of your doctors suggest that you should pay a visit to a psychiatrist. In principle, a good psychiatrist can be very helpful. But a prepotent and ignorant psychiatrist can do you a lot of damage.

For a floxie, a psychiatrist has to meet at least one previous criterium to be classified as incompetent: that he does not have a notion about toxicity of quinolones and be little inclined to study new situations posed by patients. This criterium is met by almost all psychiatrists.

Anyway, you have to be honest before your psychiatrist. So, while answering his questions, you will probably at some point tell him that:

- You are having a reaction to an antibiotic and you are ill since long ago, that symptoms do not seem to abate but sometimes they even increase; that you have cycles.
- Some or all of the tests they have done on you are clean: your blood tests, the MRIs, and so on
- Some people around you does not sympathize any longer with your situation because you look fine on the outside, so you do not talk much about it any longer.
- Some other doctors think you have fibromyalgia or nothing at all.
- You keep a carefully selected diet, avoiding aggravating foods and foods that may contain quinolones (for him clearly you see quinolones in every corner that are lying in wait for you)

But in fact he may interpret that you:

- are suffering a paranoid delusion of the somatic type, that is to say, that you harbour false beliefs about your body - for example that a physical illness exists- (your intoxication).
- that your delusion lasts for more than one month (you have been believing that since months or years ago when you discovered that cipro or levaquin is the cause of the sole cause of your miseries).
- you exhibit negative symptoms, for instance:
 - the inability to enjoy activities as much as before
 - low energy -lack of drive-
 - lack of interest in life, low motivation
 - lack of interest to socialize with other (healthy) people as before
 - social isolation spend most of the day only with close coworkers or family

Does it all sound familiar to you?. Well, bad luck, the above symptoms are the literal transcription of the full USA criteria for definitively diagnosing schizophrenia (paranoid delusion somatic type). Obviously you are going to get out of the psychiatrist office with the diagnosis tag of schizophrenic-paranoid-guy only if your psychiatrist does not give any chance to the possibility that your reaction to quinolones is real, no matter how little knowledge about it may he have, and if he does not take into account the whole picture in detail.

Some of the things that you can, and must say freely if you believe are that way, but that will reinforce his conviction that you are suffering a delusion state (paranoid) are:

- certainty (you hold your position with determination)
- incorrigibility because you do not change your idea when confronted with proof to the contrary (his educated knowledge about medicines that he is supposed to have)
- you maintain an impossibility (it is patently untrue that quinolones are benign antibiotics)
- your speech abilities are now impaired, you forget things or words, sometimes you are mentally low.
- your wife is a little weary with your situation because affects your daily habits and diet
- you do not sleep as well as before

In summary, not few floxies have ended up with a diagnosis of paranoid delirium (a sort of schizofrenia) of the somatic type (the one related to exaggerated thoughts of an illness) and their doctors have prescribed them some anti-schizofrenic drugs like aripiprazole (Abilify), clozapine (Clozaril), ziprasidone (Geodon), resperidone (Risperdal), quetiapine (Seroquel), olanzapine (Zyprexa). There are several types of brain receptors like noradrenaline, GABA, dopamine, glutamate, acetylcholine or serotonin, whose alterations can cause severe psychotic behaviours. Your dopamine receptors have degenerated and there are no other alternatives, your doctor says, and the medication is the only way out towards your cure. Those antipsychotic medications have many side effects that look very incompatible with the floxing. They can be necessary for a true paranoid or delusion disorder but surely not for you.

Think twice before you decide to take them. Looking to the experience of others, they will make you a lot worse because they block the dopamine receptors, or enhance the acetyl cholinergic effects on your brain, be it through inhibition of acetylcholine metabolism, or by acetylcholine substitution.

And do not be afraid of reassuring yourself that you are not leaving in a delusion state, but a real one. In some cases the delusion may be assumed to be false by doctor or psychiatrist assessing the belief of the patient, because it seems to be unlikely or held with excessive conviction. Psychiatrists rarely have the time or resources to check the validity of a person's claims leading to some true beliefs to be erroneously classified as delusional.

Note that the diagnoses of delusions are based on the subjective understanding of a particular psychiatrist, who may not know enough about the issue which might make a belief otherwise interpretable. So, if you are diagnosed as suffering a paranoid delusion probably it is your doctor's fault that does know close to nothing about the floxing syndrome.

50. THE TRUE BIOLOGICAL DAMAGE TO YOUR BRAIN

But the neurotransmitters more affected by your intoxication are not the dopamine receptors but the GABA (Gamma-aminobutyric acid) and cholinergic ones. In humans, GABA acts at inhibitory synapses in the brain and spinal cord. This means that whereas normal GABA function consists of landing at points (called GABA receptors) that act as brake-slowing down buttons of the nerves of the brain and spinal cord preventing the nervous system of going wildly wired, quinolones attach themselves to que GABA receptors so they impede the GABA molecules to do their job. Delirium and hallucinations associated with the fluoroquinolones have been extensively reported, particularly with levofloxacin and ciprofloxacin (because they are the most prescribed but in fact is a class effect). The proposed mechanism involved in the development of such side effects seems to be related to the quinolones' ability to inhibit the binding of GABA to the GABA receptors, leading to CENTRAL NERVOUS SYSTEM excitation.

The structural component of the fluoroquinolone molecule believed to be responsible for improved gram-positive activity is also believed to be implicated in the production of CENTRAL NERVOUS SYSTEM adverse effects. Direct proconvulsant mechanisms of quinolones may relate to gamma-aminobutyric acid (GABA)-like substituents, which act as GABA-receptor antagonists. The damage can be enhanced by the coadministration of NSAIDs and quinolones.

It would be nice that a highly toxic chemotherapeutic agent like the quinolones was very selective and only affected the GABA neuro receptors. Although not so profusely published, there are other insults the quinolones do on the neurotransmitters

Quinolones seem to have an anti-cholinergic effect (because they appear to block acetyl-choline, so that there is less availability of acetyl-choline) both at brain and peripheral levels. Central side effects of blocking acetyl-choline include confusion, disorientation, memory loss, hallucinations and paranoia. Blocking acetyl-choline in the periphery can result in a fast heart rate, dilated pupils, dry mouth, constipation, difficulty urinating, and dry skin for instance, symptoms all present in a severe reaction.

The side effects result from blocking acetyl-choline centrally, in the brain, in a region called the Nucleus Basalis. The Nucleus Basalis is related to the amygdala which orchestrates the brain's response to anxiety and fear, and the hippocampus which stores the brain's memories. So your anxiety, panic attacks and memory issues at your acute phases do not seem so unexplainable.

Well known drugs that are very hard on the acetyl-choline functioning, causing multiple health problems include antibiotics such as gentamycin, cipro, erythromycin and ampicillin, beta-blockers such as propranolol (Inderal) and timolol, calcium channel blockers such as verapamil, lithium and magnesium (many floxies cannot tolerate it) and in general anti-cholinergic drugs.

51. SOME REFLECTIONS TWO YEARS POST FLOXING

(PERMISSION PENDING)

52. A LETTER AT THREE YEARS OUT

(PERMISSION PENDING)

PART XI: YOUR DOCTORS

53. THE MAIN QUESTIONS REMAIN UNANSWERED

Apparently, there are no answers for the main questions that afflict people suffering from the floxing syndrome.

The scientific questions in desperate need of answers are:

- What are the exact mechanisms of the damage?
- Does the drug remain in the body (tissue bound) after cessation of treatment?
- Why do the most severe symptoms develop months after the treatment has ended?
- Is there a condition that makes some people more prone to being damaged?
- How deep or permanent is the neurological damage?
- Why some foods and substances trigger another amplified reaction?
- What are the irreversible internal lesions we are facing?
- What type of recovery period is to be expected?
- What can be done to limit the extent of the damage caused by these toxic chemical antibiotics?
- What can be done to help or expedite the recovery?
- What other health problems can we expect in the very long run (cancer, early morbidity, etc...)?

Obviously, there is insufficient scientific research on the subject of quinolone toxicity. And to date there is no known cure. It is difficult to understand why with so much clinical data available from us as victims and the availability of willing volunteers for studies, no scientific research is being done on a great scale. The negative influence and pressure of the drug manufacturers is the only explanation as to the reason for eluding and avoiding such desperately needed research.

From the social point of view, the critical questions about the subject are:

- Why nobody undertakes a follow up (OVER A MINIMUM PERIOD OF THREE YEARS) study of large populations of people that have taken fluoroquinolones, (especially long-term treatments) like the U.S. postal workers?
- Why the public health administrations do not begin a true, real, and accurate study, and not merely a manipulated or washed over study, about the safety of the quinolone class of antibiotics, taking into account that half of the quinolone family of antibiotics have been withdrawn from the market over the years due to severe toxicity?
- Why quinolone antibiotics are not strictly forbidden in the raising and production of cattle, poultry and fish for human consumption; because substantial amounts of the antibiotic remain in the food, irrespective of the time elapsed from administration to slaughter, and pass on to unsuspecting people?

Many thousands of people are diagnosed every year as having fibromyalgia, osteoarthritis, immune disorders and neurological problems, when in fact they are just poisoned from a quinolone, either by direct ingestion through a drug prescription or through the food supply (poultry, beef, fish, dairy).

54. WHY DOES THE MEDICAL CLASS IGNORE THE TOXICITY OF QUINOLONES

Being floxed is a very hard, life-altering experience, and sometimes a life experience of misery and accelerated physical and mental decay. You have to be prepared to add your doctor's ignorance to your despair. The average doctor, irrespective of his/her specialization, is fed technically on propaganda from the drug manufacturers. Manufacturers generously sponsor medical magazines, many medical reports, symposiums, conferences, and travel. Their advertising and information highlights the alleged benefits of quinolone antibiotics, hiding the true toxic profile.

Prescribing doctors know virtually nothing about quinolones and their use, apart from the biased information provided to them by the laboratories and drug companies, or perhaps by medical associates or other fellow physicians, that know nothing either. The main and nearly only technical information available the doctors have about these drugs comes from the advertisements in the medical magazines and visits from the drug representatives of the manufacturers. So they all think that quinolones are very safe drugs.

But the industry is one of the most dishonest that exist in the legal market. The manufacturers manipulate all the trials until they render the results (mostly forged) that they want to show. From the investigatigative work of Stephen Fried in his book "Bitter Pills":

...

A fifty seven year old woman had enrolled in an Omniflox [a quinolone] trial in october 1990 after being diagnosed with a bacterial infection on top of her chronic bronchitis. It was a double-blind trial (two unmarked drugs) and the patient initially got better. But after ten days on her study drug, she was hospitalized with kidney failure and disseminated intravascular coagulation, a life-threatening blood coagulation disorder. This was a serious dysfunction in two separate body systems. Four days later, the study "*blind*" was broken to reveal that she was taking Omniflox.

The patient's physician believed that the antibiotic had caused both of her conditions, and indeed, she recovered from both ailments, after she stopped taking the drug. However, when, as is customary, Abbott [the manufacturer] sent a letter about her case to all the other Omniflox clinical investigators who were testing the drug, the company reported her doctor's findings in a more equivocating manner, saying that the "*precise relationship of the study drug....is difficult to ascertain*" because the patient had not been "*rechallenged*".Who in their right mind would do it, except by accident? -but drug companies invariably note that is wasn't done.

As you have already learned, many people involved with the present paper have been rechallenged by a quinolone treatment, and their symptoms have always reproduced, increased in intensity dramatically, and become chronic or permanent.

More than 90% of all the prescriptions of quinolones could be avoided, using other safer, less toxic antibiotics. It is very normal and standard for urologists to prescribe a long-term course of fluoroquinolones for a suspected case of prostatitis without obtaining a culture test or a more definite diagnosis. They argue that they have a good "*penetration*" through the prostate and blood/brain barrier; so good a penetration that they wreak havoc on all bodily systems.

Let us have a look again to another passage to the book of Stephen Fried "BITTER PILLS":

While discussing antibiotic use, Blum [FDA medical officer who had approved some quinolone antibiotics] said something that stopped me in my tracks. He said authoritatively that he didn't "*perceive quinolones as first-line therapy for anything*"... "*There are definite niches where quinolones are important to have like limiting hospitalizations of patients*", he said, but for anything else, they are "*second- or third-line therapy*". I asked if he was aware that many doctors were using quinolones first. He said he was. I asked what he and other medical officers had done to let prescribing doctors know that this could be a problem. He conceded that the FDA "*had not really tried to get out*" the word on this issue.

This is the kind of information that all medical officers know, but aren't supposed to share with the public because, technically, they aren't allowed to recommend therapies. This is one of the cruelest scientific ironies of drug regulation: the only people in the world who are in a position to actually see and compare all the proprietary information on competing drugs are not permitted to tell doctors and patients what they have learned.

The arrogant ignorance of the medical class puts them in a situation prone to block any input and knowledge from their patients. The vast majority of the doctors will not listen to their patients complaining of the first signs or pains associated to the drug reaction. If your doctor tells you "it cannot be the drug" you are dealing with one of these doctors. They are firmly convinced that they behave professionally but in fact they are just frivolously superficial.

Your doctor is likely to dismiss any of your complaints if you suggest a link to the antibiotic. He will probably tell you that it is impossible, that you should never read about medical issues on the Internet, and that this is the first time he heard of something like this. He will tell you that the drug left your system long ago (perhaps it is true although quinolones can be detected in hair myelin 2 years after ingestion), and that you are somatizing your pains. If he despises your arguments, saying that you are the first person that he has met with these complaints, then he is unable to learn and cannot get beyond his limited understanding and awareness. You definitely need another doctor at this point.

A typical doctor is not willing to accept information from his/her patients. Neither he is going to rush to study or investigate your suggestions linking your alterations and the antibiotic. He does not care for them and he will not make a follow up of the evolution of his patients. There is not a single urologist or doctor that asks his patients for adverse effects one or two years after having administered them 6 weeks of ciprofloxacin (2x500mg/day), when all of them would relate the entire array of symptoms described previously in this report. In other words, he cannot discover delayed symptoms. There are reputed doctors that treat their fibromyalgia patients with quinolones; that is the same aberration as using the acid from your car's battery as eye drops for a pollen allergy. We have a strong suspicion that many fibromyalgias are caused by the ingestion of quinolones and other toxins through prescription or the diet. If you are in one of these situations you have to choose whether to follow your doctor's advice, or think twice and look for a second, or even third opinion. In the end, the only thing at stake is your life and well-being.

Many doctors do not report adverse effects to the post-marketing surveillance system. According to the most optimistic studies, it is estimated that only one in 20 adverse reactions is reported either on insistence of the patient or by the doctor's initiative. They are too busy, they are too unsure, and they do not want to be listed as too proactive in drug awareness. A floxed person needs on average 13 doctors before he/she meets one that is willing to listen that he/she was an athlete in perfect health, with rock solid joints just until the very same moment that he/she took the quinolones.

But not all doctors are equally ignorant. In the primary care system we have found quite some of them that never, under any condition prescribe a flouroquinolone because they have concluded from study and observation that they are useful but extremely toxic antibiotics that should be reserved for life or death cases.

In the scientific field there are many researchers that share the same opinion. Some medical investigations have already pointed out the shocking toxic profile of the quinolones. According to some articles that you can consult in the reference list at the end of the article, there has been an important time lag between the first reports of fluoroquinolone-related tendinopathies and the

official recognition of this toxic phenomenon. Those doctors argue that this delay, along with the widespread use of fluoroquinolones, makes it difficult to return to more reasonable prescribing guidelines for these very useful and effective antibiotics. The reasons why potentially serious adverse effects of fluoroquinolones were not anticipated before their commercialization would be related to the lack of adequate in vitro and in vivo models, and the unexpectedness of the events. Increasingly -their argument follows- fluoroquinolones are being prescribed for benign infections of the urinary or bronchial-pulmonary tracts. Sometimes, they are even used for antimicrobial prophylaxis before surgical or endoscopic procedures.

Those investigators believe that for any prescription, the risk/benefit ratio of the fluoroquinolones should be carefully considered, since better-tolerated, less expensive and less toxic drugs can usually be prescribed. Clear information dedicated both to physicians and patients regarding the cautions for use and possible adverse effects of fluoroquinolones would help reduce the risk and severity of adverse reactions. They state that this is especially important for phototoxicity, tendinopathy and cardiovascular adverse effects. We would also add the rest of extremely serious reactions described throughout this article.

And they finally identify the key error that many victims have been complaining about since the nineties: given the absence of an adequate model and the poor predictability of animal manifestations in lesions in humans, careful monitoring of patients during phase II and III trials and, more importantly, long term pharmaceutical vigilance during the post-marketing period, are an absolute need. But despite patient's and researcher's claims, it is not being done. The manufacturers of these drugs would not allow it and the FDA acquiesce.

Note:

Talk with your doctor about your concerns. Ask him to become informed because he is the person that can help you best.

If you want your doctor to cooperate you have to first convince him about the real toxic nature of the quinolone antibiotics. You will have to bring him some good papers like the ones published by Doctors Cohen and Casparian. You may get some help if he takes interest in your story.

55. SHOULD I REPORT MY REACTION

Americans are allowed to report their individual adverse events caused by drugs to the FDA through the Medwatch program. You should absolutely submit a report to Medwatch in order to create progress in promoting awareness as to the true toxicity and long-term physical disabilities caused by fluoroquinolone antibiotics. You should also insist that your doctor report it professionally as well.

Many European countries, with heavy state rules that leave very little room for individual expression and following the century's old tradition of considering citizens as poor little ignorant people prone to panicking, have suppressed any right to directly report adverse effects to the medication agencies, so it has to be done by doctors exclusively. This has been imposed by the drug manufacturers in order to get the reporting level even lower.

Once more from Stephen Fried's book "Bitter Pills":

And how bad was the ADR reporting problem? Kessler [FDA chairman] said that 90 percent of all adverse events involving drugs and devices, and perhaps as high as 99 percent of the most serious adverse events, were never reported to the FDA. The reason, he speculated, was that when doctors were confronted with an unexpected outcome of treatment, they were more likely to blame the event on "the course of the disease" than on the drug they had prescribed. He blamed this on the "limited training" that medical students receive in clinical pharmacology and drug therapy, citing a study that found only 14 percent of American medical schools required courses in the core skills needed to understand how drugs functioned in the body and properly prescribe them. Most schools "taught only a few hours of clinical pharmacology", he said, and only in the early years of training. So it was hardly surprising that prescription errors are the second most common cause of malpractice claims.

Generally speaking, doctors do not like reporting adverse reactions because of arrogance, dismissal of intellectual capability and interpretation of symptoms by their patients, self-complacency with their medical practices in the cases that they themselves prescribed the drug, fear of involvement in litigation, guilt, dislike of being involved in more future administrative work, avoidance of being characterized as too meticulous by their colleagues and the manufacturers, ignorance of the requirements for reporting, indifference about reporting mere suspicions, and lethargy.

56. THE SYSTEM IS AGAINST THE PATIENTS

The following examples, a minute sample of the real world today, illustrate that if you are affected by an adverse reaction to a quinolone antibiotic, you are going to discover a medical world full of:

CYNICISM:

When asked about the extremely severe adverse effects reported by thousands of patients Mr. MacCarthy, vice president of U.S. Medical Science at Bayer's West Haven facility states, "If you are telling me that someone had these effects and they were persisting, long term, months to years after treatment I would be surprised."

FRAUD:

(we borrow yet another excerpt from Stephen Fried's BITTER PILLS):

A rush of articles about Omniflox [a toxic quinolone] were set to appear in major journals. The company [manufacturer Abbott in this case] apparently hadn't taken any chances that the articles wouldn't toe the party line. One revealing internal memo about some of those articles described an industry practice I had heard about but never seen so clearly documented: scientific papers being written by the marketing department instead of by the scientists. Dr. Reid Patterson, Abbott's director of drug safety evaluation, was complaining in the memo about publications on Omniflox in an upcoming supplement of the American Journal of Medicine. "*Certain manuscripts*", he wrote, "*...were being labeled as being authored by more impressive, outside, expert consultants, who had nothing to do with the design or generation of the data*". In the memo Patterson, a company drug safety expert, seemed less concerned about the academic fraud than with the "*loss of recognition*" for the people who had actually done the work, as well as the possible "*impact on their advancement within Abbott*". But he was also concerned that "*marketing has decided that our data will be assembled by ghostwriters....reviewed by us, the published as though they were authored by us or by some better known consultant*".

INDOLENCE, LACK OF CARE:

In the forums you can find thousands of testimonies of persons that were dismissed by their doctors when they explained them that they were having a bad reaction to the quinolone. It is sad to read though them. Some doctors get angry at the patients, aggressive, indolent, uncaring. Others just send registered letters stating that they are no longer their doctors. All become suspicious, uneasy or hasty to get you out of their office if you mention internet. Many, ignorant of the devastation that is about coming on the patient, prescribe medications that will worsen extraordinarily their lesions (corticoids, NSAIDS, some neuroleptics).

IGNORANCE:

From the neurology forum of the Cleveland Clinic, that is a very helping and high quality board, whose questions are answered by doctors from the Clinic, consistently ranked one of the best hospitals in America:

QUESTION: I'm a 28 year old male, and recently took Cipro (4 weeks) and then Levaquin (4 weeks) for a prostate infection. I was fine on the Cipro, but started to experience muscle twitching a couple of days after switching to Levaquin. Since I've stopped taking the Levaquin (7 weeks ago), I've continued to have muscle twitching and burning muscle pain. The muscle twitching involves just a small part of the muscle and is sporadic. The twitching usually occurs in the calves, but I also notice it in the arms, back, butt, and feet. Sometimes it is just a single twitch, and other times it is a couple in a row. The burning/achy pain is somewhat all over (like after the flu), but usually in upper arms, shoulders and thighs. One of my calves also seems a little stiff, but I don't know if it's related. I can move my leg fine, just the upper part of the calf (below/around the knee) seems tight.

So far I've gone to my primary care physician, and he did some strength tests and tested my reflexes... he said all were perfectly normal, and there was no need for me to see a Neurologist. He seemed to think everything could be benign, and possibly caused by stress/anxiety. He didn't mention the Levaquin though.

My questions: Do you think my symptoms could be caused by the Levaquin? If not, what would cause them? How does stiffness start in motor neuron disease, and would it start before weakness? If I went to a Neuro, would they even do an EMG if strength and reflexes were fine?

ANSWER: I am aware of no relationship between your symptoms and Levaquin. I cannot find any references to suggest that the Levaquin caused this. It is possible that these symptoms are a reaction to a viral illness, or possible from stress (as your primary doctor suggested). If your examination is entirely normal then there may be no use for an EMG. I think it is unlikely that this represents motor neuron disease. Good luck.

As you can see, unfortunately, not even the most capable teams of doctors are informed about this real tragedy. In this case, several lay members of the forum informed adequately to the person that had suffered the reaction to levaquin.

SHEER INCOMPETENCE

Look for instance to the story of the quinolone trovafloxacin:

9th European Congress of Clinical Microbiology and Infectious Diseases. Berlin, Germany / March 21-24, 1999 The Emerging Role of Fluoroquinolones in Community-Acquired Pneumonia (CAP).

"Ten years ago I would have been howled down for including fluoroquinolones in a list of agents for the management of community-acquired pneumonia," remarked Dr. Peter Ball, Senior Lecturer at the Department of Bio-Medical Sciences, University of St. Andrews, St. Andrews, Scotland. "Why should we use these new fluoroquinolones?" Dr. Ball asked. The advantages, he answered, include excellent activity against both typical and atypical respiratory pathogens, very high penetration into tissues and fluids where the infections are centered, activity with once-daily intravenous or oral administration and excellent tolerability. Dr. Ball believes, too, that the incidence of dizziness and lightheadedness sometimes attributed to trovafloxacin is not entirely justified. "The more than 400,000 patients from post-marketing surveillance studies I have reviewed reveal this to be a very, very small problem." he said. And, he said that while sparfloxacin frequently produces skin problems attributable to phototoxicity, trovafloxacin and moxifloxacin are associated with extremely low levels of such phototoxicity.

Recognizing that dizziness/lightheadedness is the most common adverse event with trovafloxacin, particularly in young women, Dr. John Vincent, Groton, Connecticut, reported that those effects can be significantly reduced by taking the drug with food or at bedtime.

Unfortunately, it didn't occur to all those "top level" investigators to check for incapacitating neuropathies, rupturing of tendons, destruction of cartilages, or liver function during the trials, and shortly after these extraordinary claims were made, trovafloxacin was withdrawn from all European and many world countries, because of the severity of the lesions

that caused and the numbers of deaths due to fulminant liver failure.

FRIVOLITY - IRRESPONSIBILITY

PEDIATRICS Vol. 113 No. 1 January 2004, pp. e40-e46. Objective. To determine the efficacy and safety of topical ciprofloxacin/dexamethasone otic suspension compared with ofloxacin otic solution in the treatment of acute otitis media with otorrhea through tympanostomy tubes (AOMT) in pediatric patients. Group study was conducted at 39 sites in 599 children aged 6 months to 12 years with an AOMT episode of 3 weeks' duration. The mean age of patients was 2.5 years

Adverse Events: Ciprofloxacin/dexamethasone or ofloxacin administered twice daily in the affected ears is safe and well tolerated in pediatric patients with AOMT. No serious treatment-related adverse events were reported during the study. Fewer patient discontinuations as a result of adverse events were noted in the ciprofloxacin/dexamethasone group (32 patients; 5,3%) compared with ofloxacin (46 patients; 7,7%).

The safety evaluation was conducted on all patients who were randomized into the trial and received at least 1 dose of study drug. The safety analysis was based on the extent of exposure to the study drug, adverse events, and audiometry examination. The occurrence of adverse effects was assessed at each study visit and via questioning of parents or guardians during daily telephone calls relating to completion of the patient [mean age 2.5 years!] diaries. All adverse events were recorded in the patients' case report forms. Patients who experienced adverse events that, in the opinion of the investigator, presented a significant risk to their safety or well-being were withdrawn from the study. Both topical otic preparations are safe and well tolerated in pediatric patients

GREED:

Of the many tens of thousands of people with deep neurological lesions, osteoarthritis, fibromyalgias, and all the rest of damages caused by quinolones, more than 95% could have been spared if the prescription of quinolones was done properly. The rest are persons for whom the quinolones were a lifesaver, with complicated or life threatening infections. Real things are very different because of the greed of the manufacturers.

MANIPULATION:

Drug companies now spend more than \$5.5 billion to promote drugs to doctors – more than what all U.S. medical schools spend to educate medical students

Major drug companies employ about 90,000 sales representatives – one for every 4.7 doctors in the United States

The total pharmaceutical marketing budget is \$25 billion

Drug firms have spent \$800 million since 1998 buying influence, including \$675 million on direct lobbying of Congress.

No other interest group has spent more money to sway public policy

COLLUSION:

There is an outcry out there about the ever increasing evidence of the collusion between the FDA and the manufacturers. In the next section of this paper you can get a glimpse.

The positive thing is that a small part of the medical system is there to help you, if you ever find it.

PART XII: THE ROLE OF THE FOOD AND DRUG ADMINISTRATION

57. THE IMMORALITY AND INSANITY OF THE DRUG MANUFACTURERS AND THE FDA

It is beyond the scope of this article to argue in depth about the role of the FDA and the behavior of the pharmaceutical laboratories (the "industry").

But it is crystal clear that none of the people that has been surveyed for the writing of this report would have seen their lives destroyed, had their doctors known the real toxic profile of these antibiotics. Almost all the other hundreds of people that we know that have suffered proven toxic reactions to quinolones could have been treated with less toxic antibiotic for their sinusitis, sore throats or prostatitis. Probably millions of people are suffering from "fibromyalgias", all sort of pains, insomnia and neuropathies thanks to the low constant dose of quinolones (enrofloxacin mainly) ingested through food. So much of this antibiotic is currently ingested that now many people would not get any benefit of a treatment with ciprofloxacin.

We do not propose to wipe out the quinolones from the pharmaceutical arsenal, but rather disclose their true properties, so that:

- they are only used when other less toxic alternatives are not available
- they are used with the minimum dosage that works and for the minimum length of time
- they are used the least number of times along a person's lifetime
- they are completely forbidden for treatment of animals that enter the human food chain

That should be the role of the Food and Drug Administration, but they fail appallingly. Instead, like the general that sends some thousand soldiers to be slaughtered on remote hills just to erode the fighting capacity of the enemy, for the Food and Drug Administration it doesn't matter how many people are killed or disabled as far as some lives are saved in critical medical situations.

The point is that both things are compatible. Hospitals can have the quinolones for critical cases and doctors should also know their real toxicity, a thing that will only happen if the FDA discloses it.

In consequence, the FDA bears the highest responsibility in all the suffering and destroyed lives of so many tens of thousands of people. There is enough evidence that the FDA knows a lot about the quinolone toxicity epidemic that is happening, but their "client" is the *industry*, and the top officers work very much oriented towards protecting the interests of the manufacturers.

Look to a passage of the interview of Food and Drug Administration (FDA) employee and Vioxx whistleblower Dr. David Graham (the whistleblower of Vioxx), conducted by Manette Loudon:

Dr. Graham: *The FDA has a very peculiar culture. It runs like the army so it's very hierarchal. You have to go through the chain of command and if somebody up above you says that they want things done in a particular way well, they want it done in a particular way. The culture also views industry as the client.*

They're serving industry rather than the public. In fact, when a former office director for the Office of Drug Safety criticized me and tried to get me to change a report I'd written on another drug – Arava – he said to me and to a colleague who was a coauthor on this report that "industry is our client."

I begged to differ with him. I said, "No, industry is not the client, it's the American people, the people who pay our taxes. That's who we're here to serve." He said, "No! Industry is our client." I ended the conversation by saying, "Well, industry may be your client, but it will never be my client."

Dr. Graham: *..... But I've been a target of retaliation in the past. You take 10 drugs off the market well, no good deed goes unpunished at the FDA. I've experienced retaliation with many of those other episodes but not as severe as what I've experienced with Vioxx.*

This is the first time that my job was actually in jeopardy and where the FDA actually intended to fire me. That was stopped only because Sen. Grassley intervened. He put the heat on the FDA and told them, "Lay off. This guy has told the truth. He's helped America. Whose side are you on?"

There are also some books and investigative reports on the subject. We recommend "BITTER PILLS, INSIDE THE HAZARDOUS WORLD OF LEGAL DRUGS", (Bantam Publications, and author's webpage www.stephenfried.com) by Stephen Fried, whose wife suffered a mild, but debilitating, long lasting and life altering reaction to a quinolone antibiotic (Floxin).

The book will help you to learn how the "industry" is the only provider of information on medications to the FDA, how they have hidden toxic drug profiles for years, how they fail in keeping a safe program of post marketing reporting, how the laboratories spend much more on advertising and gifts than in research and safety development and how the FDA is unarmed and understaffed before all the challenges related to consumer safety.

In summary, after knowing some of the facts going on in behind the scenes and observing the experience of many friends and relatives, and our own ordeal, it is not difficult to conclude that we are subjected to corporate terrorism of low intensity and vast range, that every year ends up with many thousands of avoidable deaths and an enormous social and economic cost.

The root of the problem is in the national policies that uniformly have been opted by the ostrich model. The main guidelines of this model are:

- Deliberately trying to keep the adverse events of drugs largely unknown and unrecognized to avoid uneasiness and distress among the population, and to make the system easier to manage with low conflict.
- Fictional creation of a common notion that the system cares for us and has a drug arsenal of perfect medications.

This model causes every year 250.000 deaths due to medical errors—mostly drug related—in the United States alone. Instead of this model, one that has not been tested so far and that could save many thousands of lives would be one of clearness, truth, and simplicity. There is no reason to hide the toxic profiles of medications from citizens and doctors. It should be widely known that all drugs have undesirable adverse effects—that there are no wonder drugs; and that any given drug is intended to cure a disease but at the cost of some adverse effects on the body. It should be very clearly stated in all the drugs inserts and/or prescription notes the dosage adjustments for weight, age, body type, renal and liver function and the real figures of toxicity, classified by dosing and length of treatment, that in many cases are on average 20 to 50 times higher than currently stated. People would think twice before self-medicating and doctors would be much more responsible in their practice, carefully choosing the best alternatives and making a complete follow up of patients, with a dramatic increase in testing.

And to refresh a little for the depraved drug marketing representatives and their respective companies—all advertising should be banned as well as any visit of any doctor or rep. to another doctor with the intention of selling a medication or buying the doctor's will by any means. All non over the counter drugs (prescription drugs) would be exhaustively listed in, and only in, the apothecary books and their electronic compilations for consultation.

Some of the profits of the laboratories would go down but surely they would still be the most profitable activities in the world. And there would be much more money available for research. The market for testing would also soar up.

Unfortunately the legal drug policies seem to be forever ruled by the industry because of the corruption of the western political systems—with powerful lobbies influencing governments to act against general public interest to maximize private earnings of a few companies.

58. THEY CONTINUE TO LET THE DAMAGE OCCUR

According to the Journal of the American Medical Association (JAMA), *"Adverse drug reactions are the fourth leading cause of death in America. Reactions to prescription and over-the-counter medications kill far more people annually than all illegal drug use combined."*

Annually, drug companies spend billions on TV commercials and print media. They spend over \$12 billion a year handing out drug samples and employing sales forces to influence doctors to promote specifically branded drugs. The drug industry employs over 1,200 lobbyists, including 40 former members of Congress. Drug companies have spent close to a billion dollars since 1998 on lobbying. In 2004, drug companies and their officials contributed at least \$17 million to federal election campaigns.

Find reproduced another passage of the of the interview of Food and Drug Administration (FDA) employee and Vioxx whistleblower Dr. David Graham (the wistleblower of Vioxx), conducted by Manette Loudon (leading investigator of the team of health guru Gary Null):

Loudon: *On November 23, 2004 (during the) PBS Online News Hour Program, you were quoted as making the following statement: "I would argue that the FDA as currently configured is incapable of protecting America against another Vioxx. Simply put, FDA and the Center for Drug Evaluation Research (CDER) are broken." Since you've made that statement, has anything changed within the FDA to fix what's broken and, if not, how serious is the problem that we're dealing with here?*

Dr. Graham: *Since November, when I appeared before the Senate Finance Committee and announced to the world that the FDA was incapable of protecting America from unsafe drugs or from another Vioxx, very little has changed on the surface and substantively nothing has changed.*

The structural problems that exist within the FDA, where the people who approve the drugs are also the ones who oversee the post marketing regulation of the drug, remain unchanged. The people who approve a drug when they see that there is a safety problem with it are very reluctant to do anything about it because it will reflect badly on them. They continue to let the damage occur. America is just as at risk now as it was in November, as it was two years ago, and as it was five years ago.

Loudon: In that same PBS program, you were also quoted saying, "The organizational structure within the CDER is currently geared towards the review and approval of new drugs. When a serious safety issue arises at post marketing, the immediate reaction is almost always one of denial, rejection and heat. They approved the drugs, so there can't possibly be anything wrong with it. This is an inherent conflict of interest."

Based on what you're saying it appears that the FDA is responsible for protecting the interests of pharmaceutical companies and not the American people. Do you believe the FDA can protect the public from dangerous drugs?

Dr. Graham: As currently configured, the FDA is not able to adequately protect the American public. It's more interested in protecting the interests of industry. It views industry as its client, and the client is someone whose interest you represent. Unfortunately, that is the way the FDA is currently structured.

Within the Center for Drug Evaluation and Research, about 80 percent of the resources are geared towards the approval of new drugs and 20 percent is for everything else. Drug safety is about 5 percent. The "gorilla in the living room" is new drugs and approval. Congress has not only created that structure, they have also worsened that structure through the PDUFA, the Prescription Drug User Fee Act, by which drug companies pay money to the FDA so they will review and approve its drug. So you have that conflict as well.

Loudon: Are you at liberty to discuss some of the problems your colleagues are finding with other drugs and if so, how widespread is the problem?

Dr. Graham: I'm really not at liberty to talk about things that pertain to my official duties at the FDA. I can talk in my private capacity, but I can't talk about material that would be confidential.

What I can say is that there are a number of other scientists within the FDA who have also worked with drugs that they know are not safe, even though the FDA has approved or allowed them to remain on the market. They face some of the same difficulties that I do. The difference is that either the problem isn't as serious in terms of the numbers of people that were injured or that it's a fatal reaction – they're not willing to expose themselves to retaliation by the FDA – and retaliation would surely follow.

extracted from
[www. healthliesexposed.com](http://www.healthliesexposed.com)

59. THE REAL COST OF A CIPRO PILL

For society as a whole, the real cost of a 500 mg pill of a quinolone, taking into account the damage inflicted on so many, measured by the working hours lost, diagnostic procedures, the expenses in palliative treatments and medical bills, is not less than 800 dollars per pill, for at least 20% of those that take quinolones.

In other words, every 500 mg pill of cipro or levaquin taken in Europe and the United States has a real cost of at least 160 dollars on average. The hi-tech drug system has released a toxin that circulates disguised and freely through the primary care offices, hospitals and specialized doctors, that momentarily saves some inconveniences to the patients but that requires a huge financial effort to fix its trail of damage, and also creates a lot of human suffering.

PART XIII: I NEED A DIAGNOSIS

60. DIFFERENTIAL DIAGNOSIS

There are an array of illnesses that share common ground with the floxing syndrome (QTS) and that tend to baffle doctors. In all the cases we should consider the drug- induced version of each disorder:

- Fibromyalgia. We are not suffering from fibromyalgia, but getting such a diagnosis is at least an acknowledgement that the floxed person has a physical problem. On the contrary, many people diagnosed with fibromyalgia are really showing symptoms of a chronic intoxication caused by pharmaceutical drugs, environmental toxins or other factors.
- Multiple sclerosis, Guilliam Barré Syndrome. These two illnesses are so similar in many aspects to the QTS (quinolone toxicity syndrome) that many floxed persons are tested for them as well as for myasthenia gravis.
- Other rheumatic diseases (rheumatoid arthritis, reactive arthritis like Reiter's or spondylitis).
- Poly-myositis, dermatomyositis, inclusion body myositis.
- Steven's-Johnson syndrome.
- Serum sickness, giant cell sickness; it is well documented that cipro causes drug induced serum sickness.
- Sjogren's phenomena and syndrome; strikingly similar to QTS in so many aspects.
- Raynaud's, a localized vascular disorder.
- Small vessel vasculitis, the root problem.
- Systemic lupus erythematosus, which many floxed persons are tested for.
- Poly-neuropathy, mono-neuritis multiplex; in fact they are undeniable symptoms.
- Sensory-motor neuropathies, present in all the severe cases.
- Rhabdomyolysis, muscle destruction, with elevated CPK (creatine kinase) values.
- Toxic syndromes and neuromuscular disorders, depending on the doctors.

In some cases, the quinolones do release true autoimmune responses, so they trigger or induce real rheumatic diseases, and do cause all the illnesses listed above, as well as many others (see references at the end).

Therefore, your doctor has to conduct an elimination process in order to discern and obtain a clear diagnosis. In the best cases, you will be diagnosed as suffering from one or more of the following conditions:

- Sensory-motor, autonomic, sensory peripheral neuropathy
- Mono-neuritis multiplex, focal poly-neuropathy, especially axonal
- Peripheral neuropathy, systemic neuropathy
- Vasculitic neuropathy
- Myositis, poly-myositis, myopathies of every sort
- Myasthenic syndrome
- Vasculitis, small vessel, reactive, toxic
- Vasculitic myositis
- Cardio-myopathy
- Optic nerve myopathy, ischemic neuropathy
- Connective tissue disorder
- Tendinitis, tenosynovitis, enthesitis
- Osteoarthritis, fibromyalgia
- Leaky gut, malabsortion syndrome, candidiasis

61. MAY I HAVE A PROPER DIAGNOSIS?

No, you cannot have a proper diagnosis until the medical class recognizes the extensive toxicity of the quinolones. With almost all doctors ignorant of critical data, either because of lack of adequate education in medical school or because of later being misinformed and misguided by the advertising reports or divulgative articles paid for by -and sometimes directly written by- the manufacturers, you will not get the proper conclusion from them. Some very highly educated floxed persons, having a very distinctive healthy life prior to the floxing (which is well known to their doctors), are believed by their doctors. And, faced with the overwhelming evidence, their puzzled physicians admit that the antibiotic *"has released or created a dormant autoimmune disorder that you already had"*. **Actually**, you have a true quinolone toxicity and only an infinitesimal chance of being recognized as such. The problem is that things will not likely be oriented in the right direction by your doctor.

First of all, your doctor should report your adverse reaction to the FDA in detail. Secondly, he should ask the medical associations to which he belongs to produce more unbiased research on the toxicity of the fluoroquinolone antibiotics, and finally he should study it deeply himself. But more than a person you are a statistic, and everyday he sees many people less physically fit than you and probably with a much worse condition, even though some of them can have minor health problems but very "visible" and recognized by the medical class.

You will probably never be properly diagnosed due to the efforts of the drug manufacturers to hide, conceal and dismiss all the widespread, common and devastating injuries caused by the quinolones, and the passivity of the Food and Drug Administration (FDA) agency, that blindly believes that these reactions really amount to less than 2% of prescriptions (paradoxically the FDA officials admit that only ONE PERCENT of all adverse effects are reported).

Deprived of an accurate diagnosis, you will be classified within one of the regular, mainstream, common illnesses that doctors have heard of. And it will undoubtedly be a connective tissue disorder for a trained physician with a closed mind, or a mental psychotic or half-paranoic state if your doctor is too dumb.

It is acceptable then to start a process of elimination to rule out the main known connective tissue illnesses, starting with the main ones that have a vasculitic factor: Rheumatoid arthritis, Reactive arthritis, Systemic lupus erithematosus, Sjögren's Syndrome, Small vessel vasculitis properly speaking and following with all the rest: Fibromyalgia, Multiple sclerosis, Guilliam Barré Syndrome, Poly-myositis, Inclusion body myositis, Stevens-Johnson Syndrome, Serum sickness, Poly-neuropathy, Mononeuritis multiplex, Sensorymotor neuropathies, Rhabdomyolysis low-range, Toxic syndromes and neuromuscular disorders of every kind.

According to some doctors, who become very impressed by the neurological symptoms, the real injury is a small fiber neuropathy, both motor (axons) and sensory. Behind the small fiber neuropathy would unfaillingly be the fateful small vessel vasculitis. So, for all the neuromuscular disorders directly caused by the quinolone toxicity the precise diagnosis would be: small fiber neuropathy founded on an underlying small vessel vasculitis.

However, taking into consideration the rest of symptoms that plague floxed persons, this diagnosis falls very short of the bigger picture.

PART XIV: OTHER ANTIBIOTICS

62. I NEED TO TAKE AN ANTIBIOTIC. WHAT SHOULD I TAKE?

You are scared to death. But there is no other choice because you have a proven infection and the mild all-natural antibiotics will not clear it. This time you search frantically for a class with no adverse effects, but you do not find any. An allergic reaction to any food or drug is always possible but we do not discuss it here.

When you are floxed, any virus or bacteria that you catch will release a relapse. Your symptoms will cause you to deteriorate rapidly and in a couple of days you will find yourself months behind in your recovery. Perhaps the release of white cells into the bloodstream or other mediators alters the status of the micro-vessels, either by clogging them or by some other mechanism. So it is important to get as few infections as possible.

You have to discuss it together with your doctor and choose a class of antibiotic that is both effective against the bacteria and has as safe a profile as possible. Your search should be directed to avoid antibiotics with a high record of neurological or vasculitic adverse reactions. Medical literature has established that well: beta-lactams and the quinolones are the drugs most commonly associated with seizures and encephalopathy; the aminoglycosides, tetracyclines, clindamycin, erythromycin, polymyxins, and possibly ampicillin have the potential to aggravate neuromuscular disease; ethambutol, isoniazid, and chloramphenicol are toxic to the optic nerve; bismuth can cause a myoclonic encephalopathy, macrolids are linked especially with vasculitic events and also quinolone-wise with prolongation of the QT interval of the heart. Beta lactams have also been implicated with serum-like sickness, a condition very similar to floxing in some aspects. Sulfonamides can also release lupus, another illness that shares many similarities with the floxing syndrome. Penicillin is much studied and therefore many adverse effects have been found but it is still a choice. Some antibiotics cause total hearing loss and other severe lesions.

Never use a quinolone eye drop if another antibiotic can do the job. The quinolone will kill the bacteria for certain, but at the same time it might damage your eyes irreversibly.

There is not much left to choose from, so in the end you have to take a risk. It is unlikely that a new antibiotic of a different class will give you so much damage as the damage you are sustaining from the quinolones. Hopefully, through careful selection or by means of a couple of attempts you will find one that works well for you with no more adverse consequences.

If you have had an intermediate or severe reaction, you should put a lot of emphasis on informing doctors, nurses, emergency rooms, medical offices, and hospitals that no other quinolone antibiotic should be administered to you for the rest of your life. Indicate in your medical records that you are unable to take any fluoroquinolone antibiotics under any circumstances, as you have endured a toxic reaction and must never be exposed to them again.

63. AVOID RE-EXPOSURE TO QUINOLONES

Even if you have not been exposed to quinolones already do not take any quinolone antibiotic unless strictly necessary. Of course, do not ignore the possibility of suffering from a floxing syndrome if you have experienced the symptoms listed above and have taken quinolones in the past. One thing is clear: the effects of the quinolones are cumulative and once the reaction has been released, any rechallenge initiates an amplified response. The re-exposure will bring you devastating and possibly permanent damage that could become a life-long condition.

In any case, do not take any quinolone antibiotic unless it is absolutely necessary. Do not allow yourself to be prescribed anymore quinolone antibiotics. Quinolones are also the active agent in many non-oral formulations like eardrops, nose ointments and eyedrops.

Do not accept your doctor's prescription for a quinolone antibiotic without having checked for other alternatives and/or safer, less toxic drugs; and never take a quinolone on the grounds that "according to his experience" quinolones are effective, well tolerated, with minimal side effects as antibiotics. His experience is reduced to prescribing quinolones in the "fire and forget" manner (handing them out like candy), and not caring for the patient's adverse effects caused over time.

Remember:

After any kind of reaction, if you ever take another quinolone, the side effects can be tragic and unmanageable.

PART XV: IS THERE ANY THING THAT HELPS?

64. ADEQUATE EATING AND HABITS

Mild and intermediate reactions do not request a specific recovery program. They can more or less heal on their own. For severe reactions healthy conduct and healthy foods are all part of a recovery plan. Each of us reacts differently, and there is a lot of controversy about this issue, but on average, there is a very common core of reactions that allows us to establish some recommendations. Stick to your already healthy diet. If you develop intolerances or bad reactions to some foods (very typical), avoid them during the years to come.

Obviously, it is strongly advised to avoid any quinolone or fluoroquinolone antibiotic; and to also avoid any meat, fish, dairy, eggs or animal product that has been treated with quinolones. Some contain concentrations of quinolones that are up to 50 times higher than concentrations in human tissues during a standard treatment, and can release relapses that range from mild to very severe. Do not believe food producers or health protection agencies if they tell you that is safe to consume meat or poultry that has been kept off antibiotics for 3 days before slaughter. It is not safe, the quinolones are not fully excreted, and enough of the drug remains in the animal's tissues to bring you a very severe relapse.

*Authority: Sec. 512 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b). Sec. 20.813
Enrofloxacin oral solution.*

*(d) Conditions of use. It is used in drinking water as follows: (1) Chickens and turkeys--(i) Amount. 25 to 50 parts per million of enrofloxacin in drinking water. (ii) Indications. Chickens: Control of mortality associated with Escherichia coli susceptible to enrofloxacin. Turkeys: Control of mortality associated with E. coli and Pasteurella multocida (fowl cholera) susceptible to enrofloxacin. (iii) Limitations. Do not use in laying hens producing eggs for human consumption. Administer medicated water continuously as sole source of drinking water for 3 to 7 days. Prepare fresh stock solution daily. Treated animals must not be slaughtered for food within 2 days of the last treatment. **Individuals with a history of hypersensitivity to quinolones should avoid exposure to this product.***

During the acute phase of a severe reaction (first two years), it is quite common to feel much better when fasting for 18 hours or more. The same applies if during the fasting some probiotic cultures are taken. The improvement is felt in terms of less stiffness, less pains and less overall soreness. The original achy state returns as soon as the floxie takes any food.

A common mistake in the early stages of any floxing is to take an excessive amount of water daily. Perhaps it is not as relevant for mild or intermediate floxings but it is not recommended for severe reactions. Too much water increases the overall sickness feeling and can deplete the body from essential minerals, so hard to get through an intoxicated intestine.

Sugar has an adverse influence increasing insomnia, restlessness and neurological pains. Alcohol is also vaso-constrictive and a toxin for the neurological system, so it is better to avoid it, although clearly some wine or beer has an immediate soothing effect. Apparently tomatoes increase neurological pains, perhaps because of their acidity. On a day that the floxed person has had a predominantly acidic food, pains increase.

Caffeine is not metabolized by the floxed body so it can increase your insomnia problems. According to many reports, the floxed person cannot properly metabolize caffeine because the quinolones have damaged (extraordinarily impaired) the cytochrome P450 system that is in charge of the clearance of many drugs in the body. This explains why so many foods, additives and products cause problems to floxed persons, and why a severely affected floxed person cannot metabolize caffeine properly for at least 5 years post-floxing. Grapefruit juice has the same inhibitory effect on the cytochrome P450 system as quinolones, so it is better to avoid it.

Do not allow your cholesterol to drop too low. Some floxed persons have reported improvements with organic food high in cholesterol. However, scientific research shows that the toxic effects from these drugs on the muscle tissue acts mainly on the endogenous synthesis of cholesterol (the one produced by the body) rather than cellular uptake of preformed cholesterol (the one ingested). Maintain it a bit higher than your normal level, assuming that your normal level is ok, obviously. Note: on the short term, quinolones cause a sharp increase in the cholesterol levels (up to three fold) that tend to normalize in the first months.

Take regular supplements of omega-3 fatty acids from a reliable manufacturer. It is also beneficial to take some red peppers, garlic and onion, but do not mix large amounts of these with other supplements that they could interact negatively with or could amplify their actions. Garlic, in particular, taken in large doses (4 cloves a day) increases insomnia problems according to several

well-documented reports from floxed individuals.

The main points to address are the immune reaction and the vascular lesions. Many flare-ups are clearly linked by floxed persons with the ingestion of quinolone-containing food, but other relapses that seem to come out of the blue are in fact due to new releases of immune compounds and constrictive actions. You can act wisely if you assess every activity, food and supplement from its immunological activity and blood thinning and vaso-dilation properties. You can rate them as IgG producer, thinner, thickeners, vasodilator, vasoconstrictor or neutral. Obviously blood thinners and vasodilators will benefit you, and IgG producers, thickeners and vasoconstrictors make you prone to relapse. In all cases we are talking about habits, foods and supplements.

Remember:

Massive residues of quinolones are found in industrially raised poultry, fish and cattle; enough to cause a strong relapse.

In general, avoid cold in the extremities. It slows recovery. Take a natural, dry sauna occasionally, if you can. Avoid stressful situations and especially those that release strong emotions and feelings of anger and hate because they naturally raise cortisol levels and other hormones that target the nerves and a number of vasoactive autocooids and hormones that exert dilatory and constrictive effects resulting in negative consequences for the floxed person.

65. DRUGS THAT HELP

We do not promote taking any drug and if you need or plan to do so, then ask your doctor. Many people take drugs for neuropathic pains (Neurontin and others), normally with good or no results. Other people get benefits from heparin for its profound effects on capillary permeability and anticoagulant properties, as it increases the traffic of substrates and waste products across the interstitial compartment between cells and vessels.

Every drug that uses the P450 liver cytochrome pathway for its metabolism will probably have a detrimental or exaggerated effect on the floxed person because that mechanism is damaged by the quinolones and the concentrations of the drug can be much higher than expected.

It is better to avoid any medication that causes vasoconstriction, like anti-inflammatories (NSAIDS). If taken during months 0 to 5 they exacerbate the neurological symptoms and joint pains. There seems to be no problems with them from then on except in the event of severe floxings. In fact, NSAIDS, as many other drugs or supplements, can have a beneficial effect on mild floxings but very detrimental in severe floxings. This tends to baffle people but the reason could be simple. NSAIDS are anti-inflammatories and therefore their effect should be beneficial to all floxed persons alike. In mild and intermediate floxings, the ischemia (narrowing, flood depriving) of the blood vessels has not reached its critical point and still can take up some more narrowing before more nerves and tissues start to dye massively. However in severe floxings the critical point of ischemia has been surpassed and there is not any margin left for further vasoconstriction, and therefore small amounts of NSAIDS cause immediate pains in nerves, an exacerbation of vision issues and many more relapsing symptoms.

Inversely, floxed persons that can take some NSAIDS, soy, pinneapple, or other vasoconstrictors without relapsing or worsening their conditions, are far from their critical ischemia point and can expect an easier and quicker recovery.

Cortico-steroids may help in the first stages. They can modulate, reduce or suppress the autoimmune reaction, so they could be a treatment of choice but not for severe cases. There are medical reports indicating complete and prompt healing of quinolone reactions after some days of administration of cortisone. Many people have stated that their symptoms returned amplified once the corticoid treatment was stopped. Long-term consumption of corticoids is associated with greater risks of rupturing major tendons for floxed persons.

After the acute phases, when a severe reaction has become chronic, it is not advised to undertake any treatment for your quinolone pains based on the use of corticoids. They will exacerbate the problem, and will make tendons much more prone to rupture. Avoid anti-inflammatories as much as possible. In severe reactions anti-inflammatories always exacerbate pains in the most affected areas, while in mild reactions these negative effects might not be felt and therefore provide some relief for the pain.

Many of the commonly prescribed drugs for treating the floxing syndrome interact negatively with many natural supplements, so you should pay special attention to this fact and not mix drugs and supplements unless you are absolutely certain of their compatibility.

66. RECOMMENDED SUPPLEMENTS

For mild and intermediate reactions it is wiser not to take anything. In severe reactions the miserable quality of life for months on end exerts a lot of pressure on the search for a drug or supplement that would help in healing or to promote and expedite recovery. Out of despair, floxed persons tend to think that if an approved and hi-tech drug has brought them such a tragedy why shouldn't they look for an antidote.

Unfortunately there is not such a miracle substance; but there are some products that may help to overcome pain, chronic insomnia and disability. Supplements can be harmful too, if taken in excessive doses, if they interact with other substances or drugs you are currently taking, or simply if you are intolerant to them. You will have to avoid temptations of overdosing with vitamins and supplements, trying desperately to speed up your recovery. However, therapeutic and medically controlled doses of vitamins and supplements plus time are the only treatment advisable to date. Adjusting the dosages is a real challenge. Sometimes we stick to a very low dose and end up believing that the supplement is useless when in reality can be very helpful in higher doses. Other times we tend to take really high doses without any need for them. Always remember always that twice the normal dosage of a good thing does not double its effect and in fact can turn it in to a poison. Normally supplements should be taken a few at a time, for some weeks and then shifting to other combinations.

Very often the floxed person that has not been sufficiently informed starts taking a lot of supplements together not aware of the dangers of interactions or increased action of some combinations. Take also into account that many floxed persons are sure that the best choice is to stay away from any supplement irrespective of the severity of the reaction. Unfortunately there are contradictory experiences. For everything you plan to take, you should first consult your doctor.

Probably, the best action could be to get a blood test panel of the main ions, electrolytes, minerals and vitamins periodically, and to supplement only those that are out of balance. To make things more difficult, floxies report different results with supplements. What works fine for some is counterindicated for others. Normally those differences are seen between floxies that belong to different groups of severity of the reaction. People with the same degree of damage seem to coincide more. Anyway, based on personal experiences of some floxed persons, the following are some comments on supplements.

Central nervous system (insomnia, restlessness) and vision problems tend to benefit from foods and supplements that have blood thinning or vaso-dilatory properties. These supplements seem to be slightly detrimental for muscular pains.

For the neurological problems, long-term treatments with vitamins B1, B12, benfothiamine and vit B coenzymes may help. There is some scientific evidence that citidine plus uridine (sodium salts CMP, UTP, UDP and UMP) may help to restore the myelin sheath, but do nothing to help the motor dysfunctions. Some preparations of vitamins B can be also neurotoxic, so it is especially important not to surpass the daily-recommended doses. Many floxies report increased pains after taking vitamins of the group B.

Berry (cranberry, bilberry) extract seems to be especially effective in advanced stages of the floxing because of its modulatory effect on the smooth muscle of the blood vessels, and also its blood thinning and vasodilation capabilities. High doses can induce internal bleeding because of alterations in the quinolone-battered thinnest walls of the vasa vasorum. Other blood thinners have shown some promising therapeutic effects for floxies like ginkgo biloba, for instance. It would be interesting to find out whether a combination of one of these thinners plus magnesium taken in the early stages of a severe floxing (months 1 to 6 or so) could halt or limit the evolution of the lesions.

For vision problems, it is recommended to take some combination of vitamins A and E, plus zinc, manganese, copper and lutein. Bilberry has on its own also a very noticeable effect in making floaters less noticeable and suppressing ziggies and flashies, but tends to increase myalgias and perhaps neuropathic pains. For vision problems it is also essential to control sugar levels because quinolones cause an abnormal functioning of the adrenal glands. Sugar increases flashers, ziggies and dark flies and also insomnia.

It is well assumed that magnesium can help because of its vasodilator effect and its soothing capabilities on the nervous system. According to that, it seems important not to become magnesium deficient. There are many medical articles that show that a deficiency in magnesium levels aggravates the floxing symptoms and lesions. Some floxed persons have low serum magnesium levels. A combination of calcium and magnesium seems to work more efficiently. High doses of magnesium can have a laxative effect and for many floxed persons can exacerbate joint pains, cranks and noises, especially after some months of continued use. Not few floxed persons have their joint pains and fasciculations increase when they take magnesium (normally severely affected persons). Some vitamins are especially helpful, like vitamins C and E, but never in mega-dose preparations that are sold over the counter. As an example, vitamin E shouldn't be taken along with any blood thinner (bilberry, ginkgo, garlic) because of the risk of hemorrhage.

Coenzyme Q10 seems to be low in serum samples of some long-term floxed persons (not enough data yet). Perhaps quinolones cause the coenzyme concentrations to lower, as statins do (agents to diminish cholesterol). Then supplementation with coenzyme Q10 to maintain normal levels could be beneficial but those floxed persons that have tried it have not noticed any measurable effect. Statins have many common characteristics with quinolones. They are regarded as safe drugs too, with only a 1% to 2% rate of adverse effects, mainly musculoskeletal pains-myalgias, myopathies, neuropathies and even rhabdomyolysis (fatal muscle destruction that causes a fulminant renal collapse). But like quinolones, statins cause guaranteed damage to everybody when taken for long periods or high doses. It seems that quinolones may have a mechanism similar to the one through which statins cause their damage: decreasing the serum level of coenzyme Q10, inhibiting the conversion of HMG-CoA to mevalonic acid, both of which impair cellular integrity and reconstruction, that in turn cause destruction of muscle fibers.

To break some acute reactions, special supplementations with simple amino acids can help. Amino acids like arginine, glutamine and carnitine are usually effective in limiting some pains or progression of the symptoms. Apparently L-carnitine can help in the

restoration of nerve endings in the long run. Alpha lipoic acid is used for the neurological pains with mixed results and its role seems more related to its antioxidant activity with little adverse effects.

In many cases, quinolones create an additional problem killing the friendly bacteria of the gut, and allowing fungi to proliferate (candidiasis) as well as releasing a mal-absorption syndrome or leaky gut (damage of the lining of the intestine, impeding the normal breaking down and filtering of food elements). This syndrome poses a lot of problems in terms of lack of absorption of nutrients, toxicities and reactions to foods. It seems that the enormous net of vessels around the intestines gets damaged in severe reactions and consequently many foods provoke toxic-like reactions that are felt like exacerbations of the floxing. The lesions to the gut vessels can take a long time to heal and cause people to be in a permanent state of malaise. For this problem, some multi-minerals and multivitamins preparations (never in megadoses, avoiding "potency" products) will be helpful to replenish the normal levels of critical elements. In order to regain the natural balance of the intestinal flora, you may add some friendly lactobacillus, acidophilus or other strains to your diet.

On the other hand, insomnia, floaters and flashies increase a lot with natural anti-inflammatories or vasoconstrictors like lecithin, pineapple, sugar and other substances that are good for the joints for instance. Floxed persons seem to have a need for some nutritional joint support to help with the deterioration and the pain. Substances like MSM, glucosamine, and others are helpful in that sense but their anti-inflammatory activity increases vision problems (floaters and ziggies), the neuropathic pains, the twitchings and the heart arrhythmias and also seems to delay muscular and soft tissue recovery.

Omega 3 oils help to overcome the stiffness and the reduction in range of motion of every joint, and decrease muscle pain. Grapes (seeds) taken raw have positive effects in some mild and intermediate cases.

Recently, N-acetylcysteine, a mucolytic agent, seems to be providing good results among some floxed persons, especially among those recently intoxicated. It must be due to its vasodilator effects as it is indicated for treatments of ischemic or vasculitic toxicities. It has a low toxic profile.

Oddly enough, there are very few severely floxed persons that do not react badly to soy and its derivatives, especially if they are concentrated. Many floxed persons show high IgG antibodies against phosphatidylcholine (soy) and bromelain (pineapple). It is uncertain whether they exhibited those antibodies beforehand or it is just a consequence of the floxing. We don't know why soy (lecithin) is so bad for severely floxed persons. Probably behind this fact there is some important clue to understand one of the mechanisms of damage caused by quinolones. One of our doctors has pointed to research reports that show that phosphatidylcholine binds to bilirubin (liver waste product) creating a neurotoxic compound that has an affinity for the nerve endings. According to this doctor, floxies with normal-high or above normal levels of serum bilirubin should react worse to soy. Up to now not enough evidence has been collected as to confirm this theory.

The contents of the next table are based in the experiences of about 40 floxed persons. Not all of them have tested every one. Do not use it as a fixed frame of reference for yourself.

| -TABLE 8- POSITIVE AND NEGATIVE EFFECTS REPORTED BY FLOXED PERSONS | | |
|--|----------|----------|
| SUBSTANCE | POSITIVE | NEGATIVE |
| Magnesium | ↑↑↑ | ↓ |
| Calcium | ↑↑↑ | ↓ |
| Vitamin C | ↑↑↑ | |
| Vitamin E | ↑↑↑ | |
| Vitamins group B | ↑↑↑↑ | |
| Folate (folic acid) | ↑↑↑ | |
| Soy (phosphatidylcholine) | ↑ | ↓↓↓↓ |
| Bilberry, Cranberry | ↑↑↑↑ | ↓ |
| Bromelain | ↑ | ↓↓↓ |
| Serotonin promoters | | ↓↓↓↓ |
| Glutamine | ↑↑ | ↓↓ |
| Quercetin | ↑ | ↓↓↓ |
| Coenzyme Q10 | -- | -- |
| Tryptophan-5HTP | | ↓↓↓↓ |
| Lysine | ↑ | ↓↓ |
| Gaba | ↑↑ | ↓↓ |
| Carnitine | ↑↑↑ | |
| Gingko biloba | ↑↑↑↑ | ↓ |
| Alpha lipoic acid | ↑↑↑ | |
| Grape seed | ↑↑↑ | ↓ |
| Friendly bacteria | ↑↑ | ↓ |
| Omega 3 oils | ↑↑↑ | |
| Gamma linolenic oil (GLA) | ↑↑↑ | |
| N-acetylcysteine | ↑↑↑ | |

This is only a brief list of some of the most well known ones. There are many other substances that could be rated based on our

statistics, including minerals, all the rest of vitamins, all amino acids and many other herbal supplements, but it is beyond the scope of the current version of this report. Each substance has its own therapeutic effects. Some should not be taken together. In a future revision of this report an appendix on details about these and other supplements could be added with the point of view of the experiences of the floxed persons.

In the first instance it might be considered wise to order a test for food and supplement tolerance for every floxed person. It consists of an analysis of the IgG reactions to a hundred common foods and additives, so that the floxed person could know which ones release an IgG reaction, because such reactions could exacerbate the floxing symptoms as they would add more immune complexes to the already burdened blood vessels with the IgG and IgM complexes liberated after the toxicity. However, trials done with a few floxed persons do not show dramatic improvements if they avoid foods to which they are intolerant (IgG reactive), indicating that the drug induced immune reaction is of another order of magnitude with respect to food intolerances. In any case, lecithin –found in soy and other foods- causes very clear relapses and worsening of symptoms, but we have not yet found the causative mechanism behind it.

Remember:

*These recommendations on supplements are only comments about other's experiences.
Do not use them for planning your recovery.*

In short, is best to avoid any supplement, and adhere to a healthy diet. In any case, only people with mild and intermediate reactions can benefit from supplements, because they can choose the ones with a given effect over a specific disorder. Severely floxed people have problems with several disorders that need opposite actions. Some of the problems of a severely floxed person will exacerbate if he takes supplements for another group of lesions. So there is no other way out but time.

The suitability of taking supplements may vary along the course of the recovery. It does not seem wise to use the doses of the acute phase for long-term chronic treatments.

In summary, if you eat healthy and do not suffer from any imbalance of vitamins, minerals or electrolytes, you may consider staying away from all supplements. An alternative soft regimen for the first months of a violent reaction to quinolones could consist of taking daily some 3 x 200 mg of N-acetylcysteine and 3 x 500 mg chelated magnesium plus 2x 500 mg chelated calcium.

Detoxifying, chelating and cleansing treatments will not be discussed here. This report also does not cover any treatment by means of chemical drugs, metal compounds or the like. None of the people that have collaborated in this report has undertaken any of them.

67. PHYSICAL THERAPIES

Once more, there are no magic silver bullet treatments and no total agreement about how to treat pains and disabilities. Test the ones that help you most in maintaining your fitness and well-being. Probably some of the following will help:

- **MECHANICAL:** ultrasound; massage, especially deep massage and with the aid of steel tools by a specialized practitioner; stretching. They help with the regeneration, realignment of scar tissue and removal of by-products of the reactions. Releasing of the trigger points (entrapment of nerves in muscle bundles) that neurological deficits cause also can bring some temporary relief. Aggressive stretching of limbs affected with neuritis exacerbates neurological pains, and for some 18 hours or so, throbbing stabbing pains can be felt.
- **SUPPORTIVE:** acupuncture; relaxation, meditation, occasional dry saunas, homeopathy, mesotherapy, gentle yoga. Hyperbaric oxygen can be of help for the first stages of acute musculoskeletal collapses, when people become bedridden.
- **EXERCISE:** Especially controversial. For some it is positive only after you feel you are getting out of the acute phase: biking and swimming are preferred. Strengthening, especially isometric exercises, and several sports and exercises, should be introduced progressively. Somehow there is scattered evidence that excessive exercise can induce new relapses, which needs future clarification.

See later on the report, the section devoted to athletes.

68. INSOMNIA

Quinolones cause insomnia, that can be very radical. There are persons that cannot sleep more than 2 or 3 hours a day for 2 years and never feel the need to get asleep, no matter how collapsed their minds can get. They are wired, alert all the time.

Insomnia puts a lot of people on the verge of collapsing both physically and mentally. For many is the heaviest burden imposed by the quinolones.

Some floxies, particularly those that do not have a severe reaction, respond well to conventional man-made sleeping pills. Most severe floxies get no relief with sleeping medications.

For the first months (acute phase) nothing seems to help, neither with the insomnia, nor with the panic attacks that overwhelm people when getting momentarily asleep or eyes-wide-open distracted. Later, people can try less aggressive tactics, among which success has been reported with the following:

- herbals like hawthorn and valerian root
- aminoacids like arginine (with vitamin E and C)
- a combination of bilberry, vitamin E and probiotics
- deep breathing plus relaxation
- lowering the temperature of the limbs with the worst neurological nocturnal pains
- favoring foods with vasodilating or soothing effect: red peppers, lettuce,....
- and of course avoiding all coffee, chocolate, caffeine and sugar

PART XVI: THE END OF ANY ATHLETE'S CAREER

69. FOR ATHLETES ONLY

If you were an athlete or very active young or middle aged person, you will resume your trajectory only if you have experienced a mild reaction. Endurance will be severely curtailed by an intermediate reaction. After a severe reaction your athletic activities are completely wiped out for the next five years or so, and only then will you be in the position to attempt very physically demanding activities depending on the level of permanent damage in joints and tissues that you have sustained. In any case a severe reaction means the abrupt end of an athletic existence.

If your activities prior to the floxing was endurance athletics or vigorous professional sports, you will likely not be able to resume them ever again if you experience an intermediate or severe reaction with any joint pain at all.

There are very characteristic musculoskeletal lesions caused by quinolones. Some times they are not the worst side effects, but are big limitations for sports/physical activity and cause enormous distress in young and healthy athletes.

Cartilage is always affected. In intermediate reactions it becomes softened and some get inflamed or start causing problems; for instance in the spine, hips and knees. In severe reactions cartilage becomes very eroded, and show up as different stages of osteoarthritis, from mild to advanced. Most affected areas are the shoulder joint, hips, knees (patella, meniscus specially), and ankles, but also neck and spine.

Look at some of the musculoskeletal lesions that young and athletic floxed persons developed after unnoticed reactions to short courses of quinolones. In all cases it has been demonstrated that they were quinolone-induced toxic reactions, because after re-exposure to quinolones they increased ten to a hundred times-fold in intensity, whereas no one had had any of them before.

- Epicondylitis in tennis or racquetball players. Diagnosed as an overuse syndrome or defective techniques or equipment. In fact is a toxic tendinitis.
- Trochanteric bursitis (pain in the very tip of the hip bone). Diagnosed as tight belt syndrome or resting-on-the-side pressure. Another toxic bursitis (inflammation of the bursae, a sort of synovial bag present in most joints to help with the movements).
- Dull pain with stabbing pain episodes on the medial (inner side) or lateral (outer side) tibia, or ankle. Diagnosed as shin splints in runners and tennis players. In fact it is a neurological, tendon collapse of one or more of the tibialis complexes due to motor nerve neuropathy (toxic).
- Very commonly athletes are diagnosed as having plantar fasciitis (pain in different sections of the sole of the foot), due to supposedly hyper- or over-pronation or supination, shoe defects, leg length discrepancies, overuse, etc... It is always a toxic degradation of the muscle-tendon complex of the fascia, especially caused by neuropathic dysfunction of the anterior and posterior tibialis tendon groups.
- Hamstrings pulls are diagnosed when pain inside the hamstrings is present. This pain is not responsive to any conventional form of therapy. It is a toxic femoral neuritis (sensory-motor type). Frequently, femoral neuritis takes places in the same leg as the lower leg neuritis (ankle, tibialis). In intermediate reactions, hamstrings get involved, and to a lesser extent the antagonist muscles of the thighs. But in more severe reactions, both hamstrings and quads are affected equally and profoundly.
- Posterior tibial tendon insufficiency is in reality a result of tibial nerve dysfunction coupled with overuse and neuropathic lack of peroneal function.
- Achilles tendinitis is diagnosed hundreds of times. It is unnecessary to describe the real kind of lesion this is, as it is a very, very distinctive class effect of all quinolones. It can cause ruptured tendons quite easily. In most cases of intermediate reactions, nodules along the tendon can be palpated and well-trained operators can diagnose scarring, tearing, engrosing and fibrosing of irregular tissue from MRI images. According to some doctors, less than one in ten tendon ruptures caused by quinolones are linked to the antibiotic, because most of the ruptures take place some months after completing the treatment. The floxies whose experiences had formed this report, met doctors that had treated four physicians with ruptured tendons caused by quinolones. Only one bothered to report it.
- A cause of total collapse of one or both legs with inability to walk in severe reactions is peroneal nerve toxic motor neuropathy, very difficult to detect on the electromyograms. The lack of function of the peroneal-tibial nerves causes the surrounding muscles to experience an underperformance of their tasks, and therefore submit the tibialis and flexors tendons to increased elongation and stress, ending up in very severe lesions that normally take more than 3 years to heal. They are incorrectly diagnosed as anterior tibialis tendinitis/atrophy.
- The lack of flexing strength in some toe flexors is always a cause for concern, because it can indicate a partially

irreversible lesion in the peroneal and tibialis nerve (axonal).

- Knee pains: lateral, medial and backside. Pains in the knees caused by quinolones are of many different kinds. Neuropathic pains with a throbbing nature, increasing at night; more diffuse generalized pain due to cartilage deterioration and general tissue necrosis; localized and migrating pains due to enthesitis (tendon insertions), tendinitis and inflammation of bursae and synovial membranes.
- Back problems are innumerable. The lack of strength in all muscles, the loss of cartilage integrity, and the nerve inflammations cause myriad symptoms and pains that can be confined to the back, shoulder and neck areas or radiate and refer to other parts of the body.
- Some of the most debilitating lateral upper leg pains are diagnosed as iliotibial band syndromes. In fact they are a truly mixed toxic condition that causes: enthesitis (irritation of the end attachments), neuropathy of the femoral nerve lateral branches and gluteus nerve that control the band, a fibrotic myositis with muscle damage that loses flexibility and a fascia disorder that causes the band to adhere to the adjacent muscles due to deterioration of connective tissue.
- Iliopsoas tendinitis is diagnosed as the result of overuse because it becomes weak in most upper leg motor neuropathies. It is perceived as pain in the anterior groin, and tenderness at touch, along with some gluteus atrophy-causes an abnormal gait of being bent forward at the waist.
- The damage to all the collagenous tissues of the body can also affect all the inner joints in hips, knees and ankles.
- For the same reason as stated above, many floxings end up with torn or ruptured rotator cuff tendinitis (shoulder) as well as osteoarthritis of the shoulder joint.
- At the presentation of the floxing symptoms and the uselessness of conventional protocols, the most well trained sport physicians will suspect that something abnormal is going on. Then the floxed person could be referred to a rheumatologist and diagnosed as suffering from myopathies of several types, myositis, polymyositis and other disorders that have already been mentioned before.
- The acute muscle pains and joint stiffness after exercise can lead to an incorrect diagnosis of lactic acid building up, that can be dismissed after the corresponding tests do not indicate this.
- If you have been a strong, endurance athlete and are in your thirties or forties, your doctors will not be prone to listen your complaints about intolerance to exercise, lack of recovery, increased pains after exercise and will try to argue that it is due to the natural aging process—something that you clearly know is not the case.

70. QUINOLONES AND SPORT ARE NOT COMPATIBLE

Every athlete with a tendinitis, multi-focal muscular or neuromuscular pains or overuse syndrome, should be asked whether he/she has taken quinolones during the last year, in order to assess the diagnosis properly.

With normal fluoroquinolone treatments of one-week's worth or so, the strongest athlete will only experience a progressive diminished capacity to recover after exercise. He will feel some soreness and stiffness some hours after his exertions. He will tend to think that it is normal since no other symptoms bother him and his soreness clears up in a day or so.

With a few such short treatments of quinolones over the years, the athlete will become markedly rigid, especially in his legs. Unless he practices stretching too, he will not pay much notice either and the problem will remain unnoticed.

If an athlete takes a prolonged course of fluoroquinolones, one of his main groups of nerves (mononeuritis) can become affected, for instance the tibialis anterior and the peroneal. Then, the corresponding muscle gets wasted in a matter of a few weeks. The athlete does not realize it but his plantarflexion and his ankle dorsiflexion, respectively, become impaired. So all the stress needed to stabilize the ankle is posed on a specific group of tendons (the tibialis posterior and flexor hallucis longus for the pronators), that suddenly become completely crippled and on the verge of rupturing. The athlete and their doctors become alarmed. The doctor orders some 3-phase scans and other diagnostic procedures and reaches the wrong conclusion that the athlete suffers from asymmetries, overuses, leg length discrepancies, structural flaws and/or others. Conventional treatments are instated. The only thing that baffles everybody is the strange and disturbing long duration of the pains and limitations. Nobody has a clue about the real cause and the quinolones once again are not considered as the true cause of this toxic debilitating physical damage.

Notice that intermediate reactions predominantly affect distal motor neurons (the parts that are more distant from the trunk of the body) like ankles and wrists plus all the joints submitted to overuse, obviously. Severe reactions also affect proximal muscles and nerves (knees, hamstrings, quads, gluteus, biceps, triceps, shoulders, neck).

If an athlete has suffered a severe reaction, he loses the functionality of several joints or muscles. During the first months he can feel pains and the inability to exercise due to failure of one or two joints. But as the months pass by, more joints add to the list of incapacitating pains and limitations in range of motion. The athlete gets shocked because the list of joints involved is continuously increasing for up to 18 months and includes joints that he always had considered rock solid, without a single complaint of the slightest entity in the past. Normally, ankles, knees, hips, elbows, wrists, and shoulders are involved.

It is a tragedy for the athlete. All his joints snap and make a lot of noise when moving. Soon his knees and/or hips start grinding, clicking and cranking, normally a sign of the erosion and destruction of the cartilages. MRI's prior to and post quinolones in several athletes have shown those changes clearly, even in athletes that have refrained from exercise post-floxing.

In severe reactions there is a marked weight loss, mainly muscle. Workouts can do nothing to help recover the muscle mass, or can any supplement help, because the cause is neurological.

In severe reactions sports in cold temperatures are not advised because most likely the athlete has some toes or fingers affected by occlusive vasculitis, and the tip of some of his fingers/toes are not normally irrigated, so with temperatures hovering around freezing his tips can become numb, pale, and blue—and he risks losing some of them. Again, if the floxed person experiences some repetitive hits to his affected fingers, recovery can take a few additional years because of the superimposed damage to the vascular system caused by quinolones and subsequent mechanical injuries.

After a severe reaction it takes between 3 years (for people in their thirties) and 4 years (for people in their forties) to feel that their body is starting to recover. You will notice that the time has come when all your muscles gain strength when you exercise them. At the peak of neuropathic damage, exercise does not invigorate muscles because there is an axonal neuronal lesion not yet re-energated. But at around the third year, neurological pains in joints (hips, knees, gluteus, hamstrings, ankles) can be diminished if the athlete works out the antagonist muscles. Some times that can only be done by means of electrical stimulators at the beginning of the recovery.

Only by then will the athlete be able to start a slowly progressive program of exercises as long as he feels that his flexibility returns and also his overall recovering capacity and level of pains are improving. The athlete will also have to fight to survive the rest of symptoms affecting the heart, eyes, sinus, digestive system, insomnia, neuropathies of all kinds, etcetera, because as you have read above nearly all the organs of the body suffer disabling toxic lesions.

Every trainer, orthopedist, coach, physiotherapist and professional whose activities are related with sports should be aware of these devastating effects of the quinolone antibiotics, and advise their pupils to ask doctors for safer, less toxic alternative antibiotics.

71. WATCH OUT FOR NEW PROBLEMS. YOUR BODY IS NOT THE SAME

A floxed person is prone to suffer increased problems because the severity of many common ailments is intensified very much by the quinolone intoxication.

For instance, any time you get a virus or bacterial infection, a relapse might be released, sometimes with extraordinary virulence. Your quinolone-induced pains will increase a lot, and this situation may last for many weeks after the clearance of the bug or infection.

As explained earlier, minor traumas take an abnormally long time to recover. But a trauma on or near a floxed nerve is perhaps the worse accident that a floxed person can suffer. A floxed nerve is a nerve affected by a quinolone-induced mononeuritis, even if the floxed person had not noticed clearly that the nerve was damaged with lesions. For instance, the floxed person can have a quinolone-induced femoral neuritis but he thinks that his hip, gluteus and knee pains are just neurological pains from the antibiotic but not related to that specific nerve. If he suffers a blow on the quad that affects that nerve, the femoral neuritis will worsen sharply, and recovery of that part of the nervous system can take a few additional years of continuous and sometimes excruciating pain all along the upper leg.

The inactivity of the first months (acute phase) and above all, the quinolone neuritis that affects muscles, causes our muscles (in lean people) to atrophy a little and to lose function by a great degree. This makes things worse as our joints need as much strength as possible in order to avoid misalignments, overuse, and abuse of tendons.

For instance, without realizing it, some people, due to the severe neuropathic intoxication, and after taking it very easy with their Achilles tendons, experience atrophy of the tibialis anterior muscle, the calves, the soleus and the main ruling muscles of the lower leg and ankle. That submits the Achilles to further stress and the vicious circle starts again, leaving the Achilles or other parts of the ankle very disabled for years.

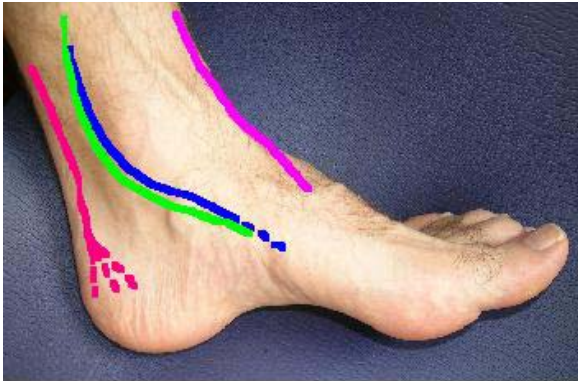
That is the reason why light weight work or isometric exercises are essential once the acute phase has passed. In severe reactions, some muscles fail to respond to strengthening exercises for at least 3 to 4 years, because the toxic neuritis that affects them makes any gain in mass or performance impossible, irrespective of the workouts that the floxed person undertakes.

Many people that suffer severe reactions develop a life-long intolerance to exercise. Any strenuous activity or sport causes their muscles to ache for a long time and their entire body becomes very stiff. It is a very common permanent aspect of internal lesions caused by quinolone antibiotics.

72. THE ANKLES: AN EXAMPLE OF TENDONS SEVERELY HIT BY QUINOLONES

In the present edition of this paper, we only deal briefly with the ankle joint and surrounding tissues, although the quinolones also

target any other joint in the body.



This picture of the ankle area shows the main tendons that are so commonly damaged by quinolones. It is a class effect, that is to say, a direct lesion, irrespective of one's build.

Red: achilles tendon.
Green: flexor digitorum longus
Blue: posterior tibial tendon
Purple: tibialis anterior



This picture shows a dorsiflexion movement. This manoeuvre stretches the achilles tendon and stresses the posterior tibial tendon and forces to work to the flexor digitorum longus.

In severe reactions, this movement done against resistance on the tip of the toes, can cause extremely incapacitating lesions in the posterior tibial and flexor digitorum group of tendons, that require months to resolve.

This same gesture plus some pronation is done during the contact phase of a normal running activity, which repetition can cause a devastating damage to the floxed athlete.

According to the studies of the mainstream, industry-prone, researchers, "*tendon disorders associated with fluoroquinolones have been estimated to occur at a rate of approximately 15 to 20 per 100,000 patients*". The real figures are those stated in table 3 of this paper, that account for 100.000 patients per 100.000 patients if they are given a high, yet approved, therapeutic dose. There is so because of a direct toxic effect.

According to the most spread manufacturer's version of this problem, out of 100 cases of achilles disorders, "*tendon rupture occurred in 31% and tendinitis in 69%*". That is again a wrong figure because ruptures are much less common than that. They also tell us that "*the average time between the start of treatment to the onset of symptoms was 13 days, with a range of 1 to 90 days*". This means that they have only studied report of ruptures associated with quinolones up to 90 days after the start of treatment, whereas in reality they occur up to many months later.

One of their studies found that 50% of patients with fluoroquinolone-induced tendinitis recovered in 1 month. In another study, 25% of the patients had symptoms that persisted for at least 2 months. So they conclude that "*even with early diagnosis and management, discontinuance of the fluoroquinolone, and placement of the tendons at rest, tendinitis heals slowly*". We would like to know how slow would they rate the healing of many athletes with unremitting and incapacitating tendinitis after 4 or 5 years of suffering.

There have been reports of patients with fluoroquinolone-associated rupture of the Achilles tendon in which histopathology was obtained. In one patient who had a rupture, the histopathology showed necrosis along with neovascularization, multiple fissures, and interstitial edema, but no inflammatory cell infiltrate. Histopathology in a second case of ruptured Achilles tendon showed necrosis and cystic changes that are not found in non-drug-associated tendinopathies.

Another patient had pain and swelling of one Achilles tendon 9 months after only a 1-week course of ciprofloxacin (500 mg bid). Biopsy of the tendon was done 4 months after the onset of symptoms. Histologic examination revealed abnormal fiber arrangement and structure with fibrotic areas, hypercellularity with some nuclei being more rounded, neovascularization, and increased glycosaminoglycans in the extracellular matrix. These histologic findings are similar to those in tendon overuse injuries in athletes.

In summary, the damage is extensive and deep, on tissues that have very little capacity to regenerate, so the lesions linger on for a long time or become chronic or permanent.

But again, for the industry and their well paid or brainwashed doctors, our group of 42 floxies, mostly young athletes with zero previous health problems, is a group of people with special risk factors prone to rupture their tendons. Read what they always add to any report on side effects of quinolones: ".....effects such as tendon ruptures, which may occur in the absence of any medication, particularly since the reported cases frequently had coexisting risk factors. However, clinical reports, histopathologic findings, and an experimental model support a causal relationship between fluoroquinolone use and tendon ruptures". ../.. "Since it is often difficult to establish causality for individual cases, efforts to quantify the risk of tendon ruptures should be viewed as only estimates. There may be a bias in overreporting an association between tendon rupture and fluoroquinolone use, involving cases that might have spontaneously occurred without the medication. On the other hand, the association may be unrecognized, and therefore some cases may be underreported". This sort of disqualification of every study makes doctors to pay no attention at all to them.

Some researchers are more independent from industry: A case report described an individual who had 9 months of symptoms after a 1-week course of fluoroquinolones: "The histopathology in this patient is particularly noteworthy. Abnormal biopsy findings, consistent with a reactive healing process, were found at 4 months, suggesting these medications may have prolonged effects on tendons. The presence of a cystic change in another patient suggests the pathophysiologic changes associated with fluoroquinolones may not be completely reversible, at least in some cases. The prolonged symptoms associated with increased glycosaminoglycans of the tendon in one patient who had only a 1-week course of antibiotics and the cystic changes in another patient support mechanisms for ruptures to occur long after the antibiotic therapy has been discontinued. An abnormal reactive healing response, or cystic degeneration, may be responsible for our case of the rupture that occurred 6 months after ciprofloxacin therapy was discontinued".

It follows: "Our cases add to the anecdotal evidence suggesting a causal relationship between fluoroquinolones and tendon rupture. Additionally, these cases highlight the broad nature of tendon ruptures that may be associated with this class of medications. Tendons other than the Achilles may be affected by the use of fluoroquinolones. Furthermore, a considerable delay may exist between the administration of a fluoroquinolone and the spontaneous rupture of a tendon. In one of our cases, the delay was 6 months after completion of a course of ciprofloxacin. However, evidence from previous reports suggests that such a delay is possible. The rat model shows that fluoroquinolones may produce inflammation of the tendon within 1 day after their administration. An abnormal healing response to fluoroquinolone-associated inflammation, or cystic degeneration may produce effects months after completion of even a short course of a fluoroquinolone"

The conclusions were: "Fluoroquinolone-associated tendon disruption, including rupture, is well described in the literature. Although the Achilles tendon is the most susceptible site, other tendons may be affected. Typically, spontaneous tendon rupture occurs during or shortly after a course of therapy, but symptoms may occur months after taking fluoroquinolones. Whether fluoroquinolones should be used in patients with a history of tendon problems or with risk factors for the development of tendon ruptures depends on the seriousness of the infection and the alternatives available. Awareness of the association between tendon disorders and fluoroquinolones may lead to enhanced surveillance, which should be extended to sites beyond the Achilles tendon and to periods of months after a course of these antibiotics".

Other problems diagnosed by means of MRI's to the floxies that participated in the forming of this paper include (for the ankle):

- tendinitis of the achilles
- tendinitis of the posterior tibial tendon, flexor digitorum and tibialis anterior
- tenosynovitis with inflammation of the tendons sheath
- synovial infiltrate on tendons
- stenosing tenosynovitis in one or more major tendons
- partial ruptures of one or more of the major tendons
- tendon cysts

Look how "mild" tendinitis and tenosynovitis look like in a young healthy athlete three years and three months after innecessary exposure to quinolones for a minor suspected bladder infection:



73. CLASSIFICATION CRITERIA FOR THE LOWER LEG

(As an example, for classification purposes, we have established a scale of severity of the tendinitis and joint problems, used to make entries in the research diaries).

The severity of the physiological performance of any given part of a floxed body is graded according to its functionality. For instance, Grade 1 corresponds to the normal state, and Grade 9 to the pre-rupture of tendons.

A floxed athlete is constantly moving from one grade to another, depending on the ingestion of more quinolones, activity level and time elapsed since last ingestion of quinolone antibiotics. Cycling of symptoms keeps floxed persons moving up and down the scale. In many cases, grade 1 is never recovered again, but instead a low, functional grade is maintained.

| -TABLE 9- CIPRO INDUCED TENDINITIS | |
|---|---|
| SCALE OF GRADES OF SEVERITY FOR THE LOWER LEG | |
| GRADE | ACTIVITY RESTRICTIONS (expressed as the maximum activity tolerated) |
| G1 | No limitations. Full sports intensity. (Normal state). There is a limited endurance in comparison with normal levels previous to the floxing. |
| G2 | There are limitations of intensity or duration of athletic activities. Maximum of 2-3 times per week for no more than 45 minutes each time. |
| G3 | Only isometric, symmetric (no lateral displacements) and non-impact sports. Avoid sudden starts and stops. Avoid especially eversion and inversion movements of the ankle. Need for a good warm up before exercising. |
| G4 | Sports play very restricted. Jogging in straight line only, no hard surfaces and level ground. Only short periods of activity allowed very few times per week. |
| G5 | Brisk walk with no limitations, including uneven ground. No uphill-downhill hiking. Only real sports possible = swimming and stationary bicycle. No sports with weight-bearing. |
| G6 | Sports forbidden at all. Not even stationary bicycle. It is not possible to walk briskly. Can walk for up to two hours but not fast. |
| G7 | Sharp and intense pain with many movements of the leg. Difficult or impossible driving. Daily activity very limited. Walk with a limp. Pains of different sorts with or without activity. |
| G8 | Claudication. Normal activities impeded. No driving. Very painful walking. Limitation of any foot movement. Pain palpable. Possible dark areas in skin. Limping. |
| G9 | Bearing weight impossible. Crutches in both arms mandatory. Foot immobilization. Pain with the smallest movement, stabbing, cutting, tearing, unbearable. Pain under pressure. Hematomas. |
| G10 | Tendon rupture or partial tear. |

NOTE: "it is not possible" really means that perhaps it is physically possible but the consequences afterwards would be a sharp worsening of symptoms, or moving to a scale higher in grade.

In intermediate reactions, the floxie moves up and down the scale many times, with a clear tendency towards recovery. For severe reactions the floxie is always between grades 3 and 9 for many years, reaching rapidly grades G6 and G7 after limited strenuous exercises, even 4 and 5 years postfloxing.

We have used other similar tables for neurological issues when preparing this report. Similar tables can help you to trace your evolution.

74. MUSCULAR DYSFUNCTION: A TREACHEROUS SEQUELAE

As repeated before, all severe reactions come with a neurological damage and many small axons are destroyed, so many muscles do not function properly. The lesions are not so profound as to cause very visible wasting of the muscles, but instead there is a marked loss of function, lack of strength, loss of muscular mass and maybe muscle destruction (high CPK and aldolase). This damages tend to be fairly asymmetrical.

The inability of some muscles to perform their tasks cause big neurological pains when tendons, joints and nerves themselves are forced to do a job for which they have become too weak. Many doctors are unable to detect manually and by exploration only this lack of strength. But athletes know their bodies too well and it is easy for them to point out the areas of disability. Special mechanical tests can measure the drop in strength of many muscles, but they are often not necessary.

For instance, a severe floxed athlete can have one weak vastus medialis plus the gluteus minimus, and perhaps the central hamstrings. This condition will increase his knee pains a lot, and besides that his neurological, shooting pains, when attempting movements with leg abduction, and running and walking in general will be much impaired.

Electrical stimulation from the 3rd year on is advisable for those muscular groups that are weak. The electrical stimulation can do nothing in terms of reversing the necrosis or dying off of the axon ends that cause muscular dysfunction, but increase a lot the strength of the surrounding fibers, and thus the overall muscular area regain some functionality that makes the pain levels to drop a lot, what allows the floxie to regain some functionality, sleep better, perhaps have less fasciculations and live with less disability. Nevertheless not even the most aggressive electrostimulating therapies are able to bring floxed muscles back to a normal shape, so they remain atrophic. As mentioned before, for a person with a strong intoxication by quinolones, it is not possible to build up

muscle no matter how hard they try to exercise. Unfortunately there some disadvantages and too much electrical discharges on the muscles can cause some breakdown and increase the CPK levels for several days.

In severe reactions, one of the best and most sensitive indicators of recovery is regaining muscle normalcy, that means normal strength and volume gain as response to exercise training.

The advantages of physical therapy is controversial for the general floxed population, but has to be seriously considered by all former athletes. It could aim the following targets:

- removal of toxins under the skin (gritty, bumpy epidermis)
- release the adherences of the fascial layers of connective tissue between muscles
- alignment of tendon fibers
- smoothing of tendon sheaths and relieving stenosing points
- increasing or maintaining the range of motion of joints
- inactivating the myofascial trigger points
- increasing muscular tone

Stretching has to be done carefully. Some stretches pose a lot of stress on the cartilage of joints and normally it is already softened by the intoxication, so scars, groves, ruptures and deep erosions can occur, whereas that would be impossible to happen in your body prior to the floxing.

75. TREAT YOUR SELF FAIRLY

Allow yourself some treats. Do not blame your bad luck. Try to keep a positive attitude. Do not submit yourself to excessively strict diets, programs or schedules.

In every phase, whenever you feel strong enough or able to, try to get in contact again with those activities that you enjoyed most before being floxed.

PART XVII: REFERENCES

76. BIBLIOGRAPHY-REFERENCES

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