Appendix 5

Medication and fluoride

There was a time when doctors thought some ailments could be improved or cured by fluoride as fluoride had been found in teeth and bones.

In 1892, Crichton-Browne recommended fluoric food for pregnant women and for children for the purpose of counteracting caries.

Brissmoret had a similar idea with regard to the osseous (the bony) system, and advocated a strengthening therapy with administration of calcium fluoride (CaF2).

In 1931, doctors Flemming Moller and Gudjonsson were suggesting the possibility of treating rarefying bone diseases found in workers at a Cryolite factory using fluorine compounds.

Other health issues were;

1) **Hyperthyroidism**. Doctors were initially excited about using fluoride as a cure for hyperthyroidism (an over-active thyroid). The fluoride certainly lowered the activity of the thyroid, but there were unfortunate adverse health side effects and the treatment often ended with a patient having no thyroid activity at all. After many years of doctors trying to perfect such a cure, it was finally abandoned.

2) **Osteoporosis**. Fluoride was proposed as a treatment for osteoporosis (porous bones, reduced bone mass or decreased bone density) as fluoride is 'calcium seeking'. Even the World Health Organisation, in 1970, reported that fluoride should be recommended, 'in high amounts during short periods of time for the treatment of osteoporosis' and, for several years. This resulted in a number of 'therapeutic' fluoride trials, included those of Kleerekoper in 1989, Hedlund and Gallagher in 1989, Riggs et al in 1990, and Danielson et al in 1992. The outcome came as a surprise, as all of them reported a significant increase in hip fractures as well as an unacceptable rate of gastrointestinal and osteoarticular side effects in the treated group compared to the controls. The conclusion was that fluoride had no place in the treatment of osteoporosis. Professor Avioli of the Washington University School of Medicine concluded as early as 1987 that:

"Sodium fluoride therapy is accompanied by so many medical complications and side effects that it is hardly worth exploring in depth as a therapeutic mode for postmenopausal osteoporosis."

(Refs: Avioli L.V. Fluoride Treatment of osteoporosis. *Postgraduate Medicine a special report* 14 September 1987 pp26-7). And (Presentation by B.L. Riggs at the International Conference on Calcium Regulating Hormones and the American Society of Bone and Mineral Research. Reported in *Medical World News* 23 October 1989 p 42.).

3) **Hip fractures.** In late 1989, the Chairman of the American FDA advisory committee reviewing fluoride's effect on (hip) fracture incidence was quoted as saying that they 'should quietly forget' about fluoride.

(Ref: Report by *Medical World News* 13 November 1989 p 25. Taken from *Fluoride*, 1992, 25:3, 162-164 article by Dr John R. Lee)

In spite of the above failures the pharmaceutical industry discovered that fluorine reinforces the action of many drugs and speeds up their intake into the body. Some of the 100s of drugs, 20 – 30% of pharmaceuticals, which contain fluoride are, anaesthetics, antibiotics, anti-cancer, antihistamines, diuretics, antacids, anti-malarial, steroids, cholesterol lowering drugs, arthritis drugs, chemotherapy drugs and tranquillizers. It is the stronger tranquillizers that contain fluoride. The tablets usually have insert information recommending that other sources of fluoride should be avoided. Fluoride can even be in vitamin drops for children.

Typically, fluoride increases the potency of drugs by about 10 times, so only about one tenth of a drug is needed to have a given effect. This is all documented in books on pharmacology by Oxford University and has been known for many years.

George Waldbott reported five infants with gastrointestinal haemorrhages who were administered fluoride vitamin drops. (Ref: Shea, J., Gillespie, S.M., and Waldbott, G.L.: Allergy to Fluoride. Ann. Allergy, 25:388-391,1967)

There is fluoride in the anti- depressant drug Prozac (or Fluoxetine). The active ingredient in the tablet is fluoxetine hydrochloride which is a compound. It is comprised of five different elements oxygen, hydrogen, carbon, nitrogen and fluorine (C17H18F3NO). The fluorine is estimated to be 18.5% of the compound. As it contains both carbon and fluorine it is an organofluorine.

(Source: National Institute of Health, (Gov).

FAN reports the following;

"The fact, however, that a pharmaceutical is made with an organofluorine does not mean that it will increase your exposure to fluoride. This is because the fluorine in the drug forms a very strong bond with the carbon and this bond resists metabolizing into fluoride ion. It is generally believed, therefore, that most organofluorine drugs do not contribute to daily fluoride exposure.

There are some organofluorine drugs, however, that do metabolize into fluoride. This is evident by studies finding elevated levels of fluoride showing up in the urine or blood following use of the drug. Because organofluorine drugs contain high quantities of fluorine, any drug that metabolizes into fluoride will likely be a very large source of daily exposure. Drugs that are known to break down into fluoride ion include: fluorinated anaesthetics, Cipro, Niflumic acid, Flecainide, and Voriconazole. It is possible, and indeed likely, that other drugs do so as well, but have not yet been discovered."

(Source: FANs website-www.fluoridealert.org).

It was from the 1980s, that fluoride started to be added to some antibiotics with disastrous results. One class of antibiotics called fluoroquinolones, with names like ciprofloxacin (trade name Cipro), moxifloxacin (Avelox) and levofloxacin (Levaquin) have come to public attention with waves of complaints from people describing a list of debilitating side-effects, from racking fatigue, mood and sensory disturbances to problems with muscles, tendons and nerve conditions which continued long after the drug was stopped. There has been a slow response to ban these products – see the information from the magazine, 'What Doctors Don't Tell You' (WDDTY), Aug. 2019 issue written by Celeste McGovern, relating the history of fluoroquinolones; full references are provided in the magazine. A short summary is given below.

By the late 1980s to 1990s, fluoroquinolones antibiotics are released on the market and, by 1993, ciprofloacin (Cipro) becomes the most frequently used antibiotic in the world.

By 1992, Temafloxacin is recalled from the market within months of its release due to numerous reports of serious adverse events, including three deaths.

In July 1999, Trovafloxacin (Trovan) use is severely restricted by the US Food and Drug Administration (FDA) after it is shown to induce serious, sometimes fatal liver damage.

In October 1999, Grepafloxacin (Raxar) is withdrawn due to its risk of 'severe cardiovascular events' including death.

In 2001, Sparfloxscin is withdrawn from US markets due to phototoxicity and a link to toxic epidermal necrolysis, a severe skin condition involving a purplish rash and blisters.

In 2008, the Food and Drug Agency (FDA) in the US attaches a black box warning to all fluoroquinolones advising of their increased risk of severe tendinitis and tendon rupture, and notes other serious adverse effects including convulsions, hallucinations, depression, serious cardiovascular events and potentially fatal diarrhoea caused by the superbug *Clostridium difficile.* It instructs doctors to use the drugs only for bacterial infections. Public Citizen, a consumer rights organisation, asks the FDA to issue doctors a warning letter along with the black box, but the FDA refuses.

In 2011, the FDA attaches a second black box warning advising of the risk of worsening muscle weakness for individuals with the autoimmune disorder myasthenia gravis.

In July 2014, the FDA requires fluoroquinolones' labels to warn of possible irreversible nerve damage.

In August 2014, an FDA review states that levofloxcin (Levaquin) is only advised for children who have inhaled anthrax or been exposed to plague (about 17 cases per year), yet reports that 68,664 paediatric prescriptions were issued between 2011 and 2014.

In 2016, the FDA requires drug makers to 'enhance' their pamphlet warnings about the association of fluoroquinolones with potentially permanent disabling side-effects involving tendons, muscles, points, nerve and central nervous system that can occur together. Mental health side-effects include memory impairment and agitation. It states that fluoroquinolones should not be used in patients with uncomplicated infections like bronchitis unless there are no other options.

In December 2017, Janssen Pharmaceuticals, a subsidiary of Johnson & Johnson, halts manufacturing of Levaquin, but says leftovers of the drug will be available until 2020. Generic versions of the drug fill the market.

In July 2018, the FDA strengthens its warnings in the prescribing information, stating that fluoroquinolones may cause low blood sugar that can result in serious problems including coma. New label changes require adding new mental health side-effects: disturbances in attention, disorientation, agitation, nervousness, memory impairment and serious delirium, even after one dose.

In Dec 2018, the FDA's latest warning: fluoroquinolones antibiotics can increase ruptures in the aorta, the main artery of the body, which can lead to dangerous bleeding and death. By 2019, at least 78,040 fluoroquinolone serious adverse events and 6,816 deaths had been reported to the FDA, including 2,840 cases in 2019.

Alan Cassels, a drug policy researcher at the University of Victoria in Canada and author of three books said: "The antibiotic issue really parallels the opioid crisis. Even though there have been the black box warnings by governments, most of the time they are just too little, too late. For their part, pharmaceutical companies are simply criminal (corporations) which break the law, pay the fine and then break the law again. The media are not as critical as they need to be, and doctors are not the gatekeepers they should be for the drugs they prescribe."

Rachel Brummer, who had suffered from such antibiotic use said:

"Drug companies have become the FDA's 'clientele', giving directives rather than being directed. It's a bit like the FDA getting half its funding from tobacco companies. Part of the reason is their funding, for example, the FDA gets 50% of its funding from Pharma."

(Refs: 'Compare two methods of measuring DNA damage induced by photogenotoxicity of fluoroquinolones'. By Zhang T., Li JL, Xin J., Ma XC, Tu Z.H. Acta Pharmacol Sin. 2004 Feb;25(2):171–5.

[Reproductive and developmental toxicity studies of sparfloxacin (2) — teratogenicity study in rats]; by H. Funabashi et al. Yakuri To Chiryo 1991 Apr;19(4):69–86.

'Effects of fluoroquinolones in a mouse limb bud culture system using regular and magnesium-deficient medium'; by R. Stahlmann et al. Teratology 1997 Jan;55(1):61–2.

'Quinolones and pregnancy: worrying animal findings, few clinical data'. Prescribe Int 1999 Feb;8(39):29–31.

'*In vitro* method for prediction of the phototoxic potentials of fluoroquinolones'; by T. Yamamoto et al. Toxicology *in Vitro* – Volume 15, Issue 6. December 2001, Pages 721–727.

'*In vitro* photochemical clastogenicity of quinolone antibacterial agents studied by a chromosomal aberration test with light irradiation'. By Satoru Itoh et al. Mutation Research/Genetic Toxicology and Environmental Mutagenesis Volume 517, Issues 1–2, 27 May 2002, Pages 113–121.)

(Bertino and Fish, 2000; Demolis et al., 1996; Dupont et al., 1996 and Owens, 2001, were withdrawn in most countries. Recently, gatifloxacin and moxifloxacin were developed as third generation of fluoroquinolones (Ball, 2000). However, in vitro studies have indicated that gatifloxacin and moxifloxacin markedly prolonged the action potential duration of the isolated guinea pig ventricular myocardium and canine Purkinje fibers (Gintant et al., 2001; Hagiwara et al., 2001 and Patmore et al., 2000). Also, gatifloxacin and moxifloxacin inhibited the human cardiac repolarizing K+ current (Anderson et al., 2001; Bischoff et al., 2000 and Kang et al., 2001). Clinical studies on the safety pharmacology of gatifloxacin and moxifloxacin indicated that these fluoroquinolones may induce QT prolongation and ventricular arrhythmias (Bertino et al., 2002; Démolis et al., 2000; Iannini and Circiumaru, 2001; Noel et al., 2003; Siepmann and Kirch, 2001 and Von Keutz and Schlüter, 1999).

('*In vivo* experimental approach for the risk assessment of fluoroquinolone antibacterial agents-induced long QT syndrome'; by Katsuyoshi Chiba et al. European Journal of Pharmacology Volume 486, Issue 2, 20 Feb. 2004, Pages 189–200.)

The new fluoroquinolones (clinafloxacin, gatifloxacin, gemifloxacin, grepafloxacin, levofloxacin, moxifloxacin, sitafloxacin, sparfloxacin and trovafloxacin) offer excellent activity against Gram-negative bacilli and improved Gram-positive activity (e.g. against Streptococcus pneumonia and Staphylococcus aureus) over ciprofloxacin... Several of these agents have either been withdrawn from the market, had their use severely restricted because of adverse effects (clinafloxacin because of phototoxicity and hypoglycaemia; grepafloxacin because of prolongation of the QTC and resultant torsades de pointes; sparfloxacin because of phototoxicity; and trovafloxacin because of hepatotoxicity), or were discontinued during developmental phases. The remaining fluoroquinolones such as gatifloxacin, gemifloxacin, levofloxacin and moxifloxacin have adverse effect profiles similar to ciprofloxacin. Extensive post–marketing safety surveillance data (as are available with ciprofloxacin and levofloxacin) are required for all new fluoroquinolones before safety can be definitively established. Drug interactions are limited; however, all fluoroquinolones interact with metal ion containing drugs (eg. antacids).

('A critical review of the fluoroquinolones: focus on respiratory infections'; by G.G. Zhanel et al. Drugs. 2002;62(1):13–59. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11790155)

"(Today), in the USA and the UK, fluoride supplements for children under the age of 6 years must be prescribed by a dentist, doctor, or health care worker. Supplements can contain 0.25 to 1 mg of fluoride per drop, tablet, or lozenge. The amount depends on the age of the child. However, in the UK it is possible to buy 0.5 mg fluoride tablets over the internet without a prescription. Supplements were designed to only be used in non-fluoridated areas as a substitute for fluoridated water. Surveys have repeatedly found, however, that some dentists prescribe supplements to children in fluoridated areas as well. Despite being prescribed for over 50 years, the Food and Drug Agency, (FDA, in the US), has never approved fluoride supplements as safe or effective."

(Source: FAN's website, www.fluoridealert.org) and ('Safety of the new fluoroquinolones compared with ciprofloxacin'. By P. Ball. J. Chemother. 2000 Jan;12 Suppl 1:8–11.)

Dr S. M. Gillespie relates the following example of harm from vitamin drops given to a child:
"C.E.O., a seven-month-old female child, had been taking Tri-Vi-Flo [vitamin drops with fluoride] daily for a week. About that time, she developed an exudative, pruritic dermatitis [itchy red skin eruptions] on the neck, face and in the antecubital and retropopliteal areas [arms and legs] accompanied by diarrhoea, abdominal cramps and bloody stools. The parents noted that the cramps occurred exclusively after the afternoon

feedings when the baby received fluoride drops. The drug was therefore discontinued. The skin immediately began to clear up. Within one week the eruption had healed, no medication had been prescribed. The child has been in good health ever since."
(Source: 'Fluoridation the Great Dilemma', by George Waldbott and 'Fluoride the Aging Factor', by John Yiamouyiannis.)

Fluoride has been a medical treatment for dental decay since the 1950s - as told in Chapter 1, while in several countries artificial fluoride as sodium fluoride or hydrofluorosilicic acid has been added to some water supplies since the mid 1940s, for the same purpose. The results of these water 'experiments', are presented in Chapter 10.

It is to be remembered that the naturally occurring calcium fluoride, (CaF_2), can be found dissolved in some water supplies where the groundwater surfaces through fluorite-containing rocks. High levels of CaF_2 have been found in drinking water in India, Africa and China. In these areas, children and people of all ages may suffer severe health problems such as crippling skeletal fluorosis and brittle bones – for photos see Appendix 2 d.

Even where calcium fluoride has been found at lower levels in drinking water, 2.0 – 2.5 ppm, such as in Colorado Springs in America, people developed brown staining to their teeth – mottled teeth, also named dental fluorosis – for an example photo see Appendix 2 b. Information on mottled teeth is given in Chapter 5