FLUORIDE & KIDNEYS

APPENDIX T

Kidney disease markedly increases an individual's susceptibility to fluoride toxicity.

The kidneys are responsible for ridding the body of ingested fluoride, and thereby preventing the buildup of toxic levels of fluoride in the body.

In healthy adults, the kidneys are able to excrete approximately 50% of an ingested dose of fluoride.

However, in adults with kidney disease the kidneys may excrete as little as 10 to 20% of an ingested dose - thus increasing the body burden of fluoride and increasing an individual's susceptibility to fluoride poisoning (e.g. renal osteodystrophy).

The bone changes commonly found among patients with advanced kidney disease closely resemble the bone changes found among individuals with the osteomalacic-type of skeletal fluorosis. This raises the possibility that some individuals with kidney disease are suffering from undiagnosed skeletal fluorosis.

As noted by Dr. Edward Groth, a veteran Senior Scientist at Consumers Union:

"It seems probable that some people with severe or long-term renal disease, which might not be advanced enough to require hemodialysis, can still experience reduced fluoride excretion to an extent that can lead to fluorosis, or aggravate skeletal complications associated with kidney disease... It has been estimated that one in every 25 Americans may have some form of kidney disease; it would seem imperative that the magnitude of risk to such a large sub-segment of the population be determined through extensive and careful study. To date, however, no studies of this sort have been carried out, and none is planned" (Groth 1973; Doctoral Thesis; Stanford University).

Because the kidney accumulates more fluoride than all other soft tissues (with the exception of the pineal gland), there is concern that excess fluoride exposure may contribute to kidney disease - thus initiating a "vicious cycle" where the damaged kidneys increase the accumulation of fluoride, causing in turn further damage to the kidney, bone, and other organs.

The possibility that fluoride exposure can cause direct damage to kidney tissue is supported by a long line of animal and human studies.

In studies on fluoride-exposed animals, kidney damage has been reported at levels as low as 1 ppm if the animals consume the water for long periods of time.

In humans, elevated rates of kidney damage are frequently encountered among populations with skeletal fluorosis. In addition, several case reports suggest that some individuals with

kidney disease can experience significant recovery in their clinical signs and symptoms following the provision of fluoride-free water.

VIDEO: **Fluoride Risks for Kidney Patients** (see also ***YouTube version***)

Fluoride & the Kidneys - **Studies Available Online:** (back to top)

EXCERPT - html: Johnson W, et al. (1979). *Fluoridation and bone disease in renal patients*. In: E Johansen, DR Taves, TO Olsen, Eds. Continuing Evaluation of the Use of Fluorides. AAAS Selected Symposium. Westview Press, Boulder, Colorado. pp. 275-293.

Fluoride & the Kidneys - Articles of Interest: (back to top)

- National Kidney Foundation Admits: Kidney Patients Should be Notified of Potential Risk from Fluorides and Fluoridated Drinking Water - The Lillie Center, June 3, 2008
- Utility official sees wife's health approve since fluoride dropped - *The Daily Times, Maryville, Tennessee; April 4, 2005*

Fluoride & the Kidneys - Kidney Patients at Increased Risk of Fluoride Poisoning: (back to top)

1. "Epithelia in lung, skin, and kidney are often exposed to fluoride, and tissue damage in lung and kidney due to fluoride is well documented. Nevertheless, the biological effects of fluoride on epithelia are poorly investigated. In the present study, we report effects of sodium fluoride (NaF) on the differentiation of a human epithelial cell line, HaCaT. These cells may serve as a keratinocyte model, because they express a wide spectrum of keratins (Ks), and they associate into stratified tissue-like arrangements along with changes in their keratin pattern. NaF was added to the culture medium at concentrations of 0.5 and 5 mM. . . . The changes in keratin expression were not reversed by withdrawal of fluoride. Taken together, NaF at high dose blocked terminal differentiation of HaCaT cells, visible by keratin expression and failing stratification. This effect may disturb tissue formation due to altered cell interactions." Prado E, Wurtz T, Ferbus D, Shabana EH, Forest N, Berdal A. Sodium fluoride influences the expression of keratins in cultured keratinocytes. Cell Biol Toxicol. 2010 Aug 1

2. "Fluoride, of all inorganic substances, is among the least likely to be identified by a routine toxicological analysis. Acute poisonings with salts of hydrofluoric or fluorosilicic acid, however, although relatively uncommon, may occur. . . . In the first case, the results were: blood - 130mugF/ml, stomach - 1150mugF/g, small intestine content - 19.6mugF/g, kidney - 56.0mugF/g, and urine - 1940mugF/ml. In the second case, the contents of fluorine and zinc in blood and internal organs were the following: blood - 6.03mugF/ml, 23.8mugZn/ml; brain - 1.39mugF/g, 7.54mugZn/g; stomach - 152mugZn/g; stomach content - 293mugF/g, 84.4mugZn/g; small intestine - 37.5mugZn/g; small intestine content - 63.4mugF/g, 19.6mugZn/g; liver - 9.49mugF/g, 81.0mugZn/g; kidney - 29.6mugF/g, 39.2mugZn/g; and exceeded the normal levels of these elements in biological material many times." Lech T. Fatal

cases of acute suicidal sodium and accidental zinc fluorosilicate poisoning. Review of acute intoxications due to fluoride compounds. Forensic Sci Int. 2010 Jul 22.

3. "Therefore it can be concluded that black berry administration could minimize the toxic effects of fluoride indicating its free radical-scavenging and potent anti-oxidant activities." Hassan HA, Abdel-Aziz AF., Food Chem Toxicol. Evaluation of free radical-scavenging and anti-oxidant properties of black berry against fluoride toxicity in rats. 2010 Aug-Sep;48(8-9):1999-2004. Epub 2010 May 22.

4. "Rats received a single intravenous injection of HFA (3.2, 6.4, or 9.6 (LD(5)) mg/kg) or saline. . . . Conclusions: We consider that acute nephrotoxicity of HFA caused renal injury, and the harmful effects of HFA were subsequently aggravated by its delayed metabolism." **Mitsui G, Dote T, Yamadori E, Imanishi M, Nakayama S, Ohnishi K, Kono K. Toxicokinetics and Metabolism Deteriorated by Acute Nephrotoxicity after a Single Intravenous Injection of Hydrofluoric Acid in Rats. J Occup Health. 2010 Oct 12**

5. "The results indicate that the affected regions contain moderate to high levels of fluoride." Chronic kidney diseases of uncertain etiology (CKDue) in Sri Lanka: geographic distribution and environmental implications. **Chandrajith R**, **Nanayakkara S**, **Itai K**, **Aturaliya TN**, **Dissanayake CB**, **Abeysekera T**, **Harada K**, **Watanabe T**, **Koizumi A**. **Environ Geochem Health.** 2010 Sep 18.

6. "These data suggest that oim (Osteogenesis imperfecta murine) mice have reduced bone strength due to homotrimeric type I collagen, independent of bone fluoride content." Carleton SM, Whitford GM, Phillips CL. Dietary fluoride restriction does not alter femoral biomechanical strength in col1a2-deficient (oim) mice with type I collagen glomerulopathy. J Nutr. 2010 Oct;140(10):1752-6. Epub 2010 Aug 19.

7. "Selective low (15 mg sodium fluoride (NaF)/L) and relatively high (150 mg NaF/L) doses of in vivo fluoride (F) treatment to Swiss albino mice through drinking water elicited organ-specific toxicological response. All the F-exposed groups showed severe alterations in both liver and kidney architectures, but there was no significant change in the rate of water consumption and body weight." Chattopadhyay A, Podder S, Agarwal S, Bhattacharya S. Fluoride-induced histopathology and synthesis of stress protein in liver and kidney of mice. Arch Toxicol. 2010 Sep 22. [Epub ahead of print]

8. "[A] fairly substantial body of research indicates that patients with chronic renal insufficiency are at an increased risk of chronic fluoride toxicity. Patients with reduced glomerular filtration rates have a decreased ability to excrete fluoride in the urine. These patients may develop skeletal fluorosis even at 1 ppm fluoride in the drinking water... The National Kidney Foundation in its 'Position Paper on Fluoride—1980' as well as the Kidney Health Australia express concern about fluoride retention in kidney patients. They caution physicians to monitor the fluoride intake of patients with advanced stages of kidney diseases. However, a number of reasons will account for the failure to monitor fluoride intake in patients with stages 4 and 5 of chronic kidney diseases and to detect early effects of fluoride retention on kidneys and bone. The safety margin for exposure to fluoride by renal patients is unknown, measurements of fluoride levels are not routine, the onset of skeletal fluorosis is slow and insidious, clinical symptoms of this skeletal disorder are vague, progression of renal functional

decline is multifactorial and physicians are unaware of side effects of fluoride on kidneys or bone."
SOURCE: Schiffl H. (2008). Fluoridation of drinking water and chronic kidney disease: absence of evidence is not evidence of absence. Nephrology Dialysis Transplantation 23:411.

9. "Individuals with kidney disease have decreased ability to excrete fluoride in urine and are at risk of developing fluorosis even at normal recommended limit of 0.7 to 1.2 mg/l."
SOURCE: Bansal R, Tiwari SC. (2006). Back pain in chronic renal failure. Nephrology Dialysis Transplantation 21:2331-2332.

10. "Persons with renal failure can have a four fold increase in skeletal fluoride content, are at more risk of spontaneous bone fractures, and akin to skeletal fluorosis even at 1.0 ppm fluoride in drinking water."
SOURCE: Ayoob S, Gupta AK. (2006). Fluoride in Drinking Water: A Review on the Status and Stress Effects. Critical Reviews in Environmental Science and Technology 36:433–487

11. "In patients with reduced renal function, the potential for fluoride accumulation in the skeleton is increased. It has been known for many years that people with renal insufficiency have elevated plasma fluoride concentrations compared with normal healthy persons and are at a higher risk of developing skeletal fluorosis."
SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p140 .

12. "Skeletal fluorosis seems possible, especially in hot climates or with renal compromise, from drinking excessive quantities of instant or bottled teas. Our observations support the need for better understanding of the amounts and systemic effects of fluoride in teas."
SOURCE: Whyte M. (2006). Fluoride levels in bottled teas. American Journal of Medicine 119:189-190.

13. "We hypothesize that elevated serum F levels might contribute to the disturbances in mineral ion homeostasis that are observed in patients with CRI [Chronic Renal Insufficiency]. This is of particular concern since the incidence of dental fluorosis has increased due to increased F– uptake from multiple fluoridated sources. The ubiquitous presence of F in food and beverage products regardless of the degree of water fluoridation suggests that the overall F exposure in individuals with CRI may need to be more closely monitored."
SOURCE: Mathias RS, et al. (2000). Increased fluoride content in the femur growth plate and cortical bone of uremic rats. Pediatric Nephrology 14:935–939

14. “It is important to control the intake of this element [fluoride] and the prolonged use of fluoridated dental products in the subjects with chronic renal insufficiency, to avoid a risk of fluorosis.”
SOURCE: Torra M, et al. (1998). Serum and urine fluoride concentration: relationships to age, sex and renal function in a non-fluoridated population. Science of the Total Environment 220: 81-5.

15. "[A] fairly substantial body of research indicates that people with kidney dysfunction are at increased risk of developing some degree of skeletal fluorosis. ... However, there has been no systematic survey of people with impaired kidney function to determine how many actually suffer a degree of skeletal fluorosis that is clearly detrimental to their health."
SOURCE: Hileman B. (1988). Fluoridation of water.Questions about health risks and benefits remain after more than 40 years. Chemical and Engineering News August 1, 1988, 26-42.

16. "It seems probable that some people with severe or long-term renal disease, which might not be advanced enough to require hemodialysis, can still experience reduced fluoride excretion to an extent that can lead to fluorosis, or aggravate skeletal complications associated with kidney disease... It has been estimated that one in every 25 Americans may have some form of kidney disease; it would seem imperative that the magnitude of risk to such a large sub-segment of the population be determined through extensive and careful study. To date, however, no studies of this sort have been carried out, and none is planned."
SOURCE: Groth, E. (1973). Two Issues of Science and Public Policy: Air Pollution Control in the San Francisco Bay Area, and Fluoridation of Community Water Supplies. Ph.D. Dissertation, Department of Biological Sciences, Stanford University, May 1973.

17. "It would not be surprising if there were some undetected cases of skeletal fluorosis in the Australian population in individuals with pathological thirst disorders and/or impaired renal function. However, the matter has not been systematically examined. This matter should be the subject of careful and systematic review."
SOURCE: National Health and Medical Research Council. (1991). The effectiveness of water fluoridation. Canberra, Australia: Australian Government Publishing Service.

18. "Though fluorosis is prevalent in certain geographic parts of the world, it is likely to occur in other parts... in people with latent kidney disease even when they consume relatively lower amounts of fluoride than in endemic regions."
SOURCE: Reddy DR, et al. (1993). Neuro-radiology of skeletal fluorosis. Annals of the Academy of Medicine, Singapore 22(3 Suppl):493-500.

19. "Impairment of renal function can prolong the plasma half-life and contribute to clinical toxicity at lower concentrations of fluoride intake."
SOURCE: Fisher RL, et al. (1989). Endemic fluorosis with spinal cord compression. A case report and review. Archives of Internal Medicine 149: 697-700.

20. "Persons with chronic renal failures constitute a possible group at-risk with respect to the occurrence of skeletal fluorosis, because of an increased fluoride retention after oral intake. Based on the results of one study, in which the difference in retention between nephritic patients and healthy persons was quantified (average retention: 65% and 20%, respectively), a total daily intake of about 1.5 mg appears to be the maximum acceptable intake for nephritic patients. In view of the limitations of this comparative study and of the individual differences in retention and sensitivity, this figure must only be regarded as an indication."
SOURCE: National Institute for Public Health and Environmental Protection. (1989). Integrated criteria document fluorides. Report No 758474010. The Netherlands.

21. "The skeletal complication of fluoride is more common in renal disease. Because of the impairment in renal excretion of fluoride, high circulating concentrations of fluoride may be

achieved in renal disease."
SOURCE: Pak CY. (1989). Fluoride and osteoporosis. Proceedings of the Society for Experimental Biology and Medicine 191: 278-86.

22. "Fluoridation of drinking water up to 1.2 ppm apparently does not pose a potential risk to bone provided the renal function is normal... We should, however, recognize that it is difficult to give a strict value for a safe fluoride concentration in drinking water, because individual susceptibility to fluoride varies."
SOURCE: Arnala I, et al. (1985). Effects of fluoride on bone in Finland. Histomorphometry of cadaver bone from low and high fluoride areas. Acta Orthopaedica Scandinavica 56(2):161-6.

23. "Because the kidney is the main pathway of fluoride excretion, patients with chronic renal failure are especially vulnerable to osseous accumulation of ingested fluoride and to potentially deleterious effects."
SOURCE: Fisher JR, et al. (1981). Skeletal fluorosis from eating soil. Arizona Medicine 38: 833-5.

24. "The finding of adverse effects in (kidney) patients drinking water with 2 ppm of fluoride suggests that a few similar cases may be found in patients imbibing 1 ppm, especially if large volumes are consumed, or in heavy tea drinkers and if fluoride is indeed the cause."
SOURCE: Johnson W, et al. (1979). Fluoridation and bone disease in renal patients. In: E Johansen, DR Taves, TO Olsen, Eds. Continuing Evaluation of the Use of Fluorides. AAAS Selected Symposium. Westview Press, Boulder, Colorado. pp. 275-293.

25. "In the human body, the kidneys are probably the most crucial organ during the course of low-dose long-term exposure to fluoride. Healthy kidneys excrete 50 to 60% of the ingested dose (Marier and Rose 1971). Kidney malfunction can impede this excretion, thereby causing an increased deposition of fluoride into bone. Marier (1977) has reviewed data showing that, in persons with advanced bilateral pyelonephritis, the skeletal fluoride content can be 4-fold that of similarly-exposed persons with normal kidneys. Similarly, Mernagh et al. (1977) have reported a 4-fold higher skeletal fluoride content in persons with the renal failure of osteodystrophy. It has also been shown (Seidenberg et al. 1976; Hanhijarvi 1975) that plasma F- levels can be 3 1/2 to 5 times higher than normal in persons with renal insufficiency. It is thus apparent that persons afflicted with some types of kidney malfunction constitute another group that is more "at risk" than is the general population."
SOURCE: Marier J, Rose D. (1977). Environmental Fluoride. National Research Council of Canada. Associate Committe on Scientific Criteria for Environmental Quality. NRCC No. 16081.

26. "It is generally agreed that water fluoridation is safe for persons with normal kidneys. Systemic fluorosis in patients with diminished renal function, however, seems a reasonable possibility. In such patients, fluoride may be retained with resulting higher tissue fluoride levels than in persons with normal renal function."
SOURCE: Juncos LI, Donadio JV. (1972). Renal failure and fluorosis. Journal of the American Medical Association 222:783-5.

27. "Prolonged polydipsia (excessive thirst) may be hazardous to persons who live in areas where the levels of fluoride in drinking water are not those usually associated with significant fluorosis."

SOURCE: Sauerbrunn BJ, et al. (1965). Chronic fluoride intoxication with fluorotic radiculomyelopathy. Annals of Internal Medicine 63: 1074-1078.

28. "The question of the effect of water containing 1 p.p.m. upon patients with severe impairment of kidney function requires special consideration in view of the fact that radiologic evidence of chronic fluorosis has been found in two persons with severe kidney disease who died at the early ages of 22 and 23 years, respectively..."
SOURCE: Heyroth F. (1952). Hearings Before the House Select Committee to Investigate the Use of Chemicals in Foods and Cosmetics, House of Representatives, 82nd Congress, Part 3, Washington D.C., Government Printing Office, p. 28.

29. "All patients with dental fluorosis and anemia and/or signs of renal impairment should have radiographic examinations of the skeletal system to rule out the existence of fluoride osteosclerosis... It is likely that the reason our patient retained fluorine in his bones was that he had renal damage of long standing; without this the osteosclerosis might not have developed."
SOURCE: Linsman JF, McMurray CA. (1943). Fluoride osteosclerosis from drinking water. Radiology 40: 474-484.

30. "Fluoride is bone-seeking due to its high affinity for calcium phosphate and therefore accumulates in bone. Radiological changes can be quite similar to changes of renal osteodystrophy, and therefore the diagnosis may be missed unless specifically investigated."
SOURCE: Bansal R, Tiwari SC. (2006). Back pain in chronic renal failure. Nephrology Dialysis Transplantation 21:2331-2332.

31. "[R]enal disease and fluoride cause similar changes. This overlap makes it very difficult to assess the effect of fluoride per se in these patients."
SOURCE: Johnson W, et al. (1979). Fluoridation and bone disease in renal patients. In: E Johansen, DR Taves, TO Olsen, Eds. Continuing Evaluation of the Use of Fluorides. AAAS Selected Symposium. Westview Press, Boulder, Colorado. pp. 275-293.

32. "The findings of osteosclerosis, osteomalacia and increased bone resorption have been confirmed in experimental fluorosis in animals. It can be seen, therefore, that fluoride bone disease could mimic renal osteodystrophy."
SOURCE: Cordy PE, et al. (1974). Bone disease in hemodialysis patients with particular reference to the effect of fluoride. Transactions of the American Society of Artifical Internal Organs 20: 197-202.

33. "[T]he observed changes (osteomalacia, osteitis fibrosa and osteoporosis) were similar to those induced by high doses of fluoride in humans and experimental animals, in which widened osteoid seams have been observed, and where increased areas of resorption due to secondary hyperparathyroidism may be seen."
SOURCE: Posen GA, et al. (1971). Renal osteodystrophy in patients on long-term hemodialysis with fluoridated water. Fluoride 4: 114- 128.

34. "Osteosclerosis from chronic renal disease associated with secondary hyperparathyroidism may produce similar changes (as fluorosis), and indeed may have intensified the findings (of fluorosis) in one of our patients."

SOURCE: Morris JW. (1965). Skeletal fluorosis among indians of the American Southwest. American Journal of Roentgenology, Radium Therapy & Nuclear Medicine 94: 608-615.

35. In the fluoride-treated patients, "we observed osteoclasts resorbing bone beneath osteoid seams, and fragments of osteoid isolated in the bone marrow. This type of resorption beneath unmineralized bone matrix is often observed in osteomalacia, particularly that caused by renal abnormalities and associated secondary hyperparathyroidism."
SOURCE: Lundy MW, et al. (1995). Histomophometric analysis of iliac crest bone biopsies in placebo-treated versus fluoride-treated subjects. Osteoporosis International 5:115-129.

36. "During our field studies our attention was drawn to the high incidence of bone disease and bony leg deformities with clinical invalidism in children exposed to high intake of endemic fluoride in drinking water. Due to variable and unusual clinical features, these children (with fluorosis) had often been mistaken for rickets, renal osteodystrophy, osteosclerosis and hereditary osteopathies etc."
SOURCE: Teotia M, Teotia SP, Singh KP. (1998). Endemic chronic fluoride toxicity and dietary calcium deficiency interaction syndromes of metabolic bone disease and deformities in India: year 2000. Indian Journal of Pediatrics 65:371-81.

37. "A 40-year-old American Indian woman with chronic pyelonephritis and renal failure complained of progressive muscular weakness, fatigue, and increasingly severe pain in her ribs, low back, and left hip. X-ray study of these areas showed evidence of osteosclerosis, compatible with either renal osteodystrophy or skeletal fluorosis... No other pathologic changes were apparent in the bones or ligaments..."
SOURCE: Fisher JR, et al. (1981). Skeletal fluorosis from eating soil. Arizona Medicine 38: 833-5.

38. “Human kidneys... concentrate fluoride as much as 50-fold from plasma to urine. Portions of the renal system may therefore be at higher risk of fluoride toxicity than most soft tissues.”
SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p236.

39. "Based on these studies it is known that, among soft tissues, the kidney has the highest fluoride concentrations. This is mainly attributable to high concentrations within the tubular and interstitial fluids in the medullary papillary regions."
SOURCE: Whitford G. (1996). The Metabolism and Toxicity of Fluoride. 2nd Revised Edition. Karger: Basel. p 30.
(NOTE: Since the publication of this report, it has been discovered that the soft tissue of the pineal gland contains higher fluoride levels than the kidney.)

40. "Effects in the kidneys are of the first to be seen in fluoride exposure of mammals. The reason for this is considered to be the relative high concentrations of fluoride found in the kidneys and in the urine during exposure."
SOURCE: Hongslo CF, Hongslo JK, Holland RI. (1980). Fluoride sensitivity of cells from different organs. Acta Pharmacologica et Toxicologica 46:73-77.

41. "OBJECTIVE: To explore the dose-effect relationship of water fluoride levels and renal damage in children and observe the difference of renal function between high-loaded fluoride people and dental fluorosis people in the same water fluoride level region. METHODS: 210 children were divided into seven groups in term of drinking water fluoride levels and whether they suffered from dental fluorosis. Fluoride concentrations in urine and serum and activities of urine NAG and gamma-GT were determined. RESULTS: The urine and serum fluoride of high-loaded fluoride people and dental fluorosis people increased compared with control, moreover fluoride contents in urine and serum increased gradually with the increase of fluoride level in drinking water. Urine NAG and gamma-GT activities significantly increased in dental fluorosis people from area of 2.58 mg/L fluoride in drinking water and in those two groups from area of 4.51 mg/L fluoride in drinking water. Moreover, there existed an obvious dose-effect relationship between the drinking water fluoride concentration and NAG and gamma-GT activity. CONCLUSION: Over 2.0 mg/L fluoride in drinking water can cause renal damage in children, and the damage degree increases with the dinking water fluoride content. Renal damage degree is not related to whether the children suffered from dental fluorosis and mainly due to water fluoride concentration."
SOURCE: Liu JL, Xia T, Yu YY, Sun XZ, Zhu Q, He W, Zhang M, Wang A. (2005). [The dose-effect relationship of water fluoride levels and renal damage in children] Wei Sheng Yan Jiu. 34(3):287-8.

42. "In my medical practice I have encountered two cases in which fluoridated water interfered with kidney function. One of these, Miss G.L., 27 years old, had been under my care from July 1966 to September 1969 for allergic nasal and sinus disease. She had a congenital cystic kidney necessitating consultation with a urologist. As shown by its inability to excrete indigo carmine, a dye employed as an indicator of kidney function, the left kidney was not working and was slated for removal. This patient also reported having pains and numbness in arms and legs, spasticity of the bowels, ulcers in the mouth, headaches, and a progressive general disability - symptoms of possible intolerance to fluoride - for about 15 years. Her water supply (Highland Park, Michigan) had been fluoridated since September 1952. On February 1, 1967, I instructed her to avoid fluoridated water for drinking and cooking. Within a few weeks all the above-mentioned symptoms disappeared, and another kidney dye test on June 12, 1967, astonishingly revealed that the left kidney had begun to function again! A follow-up 5 years later revealed that the patient had remained in good health as long as she refrained from drinking fluoridated water.

43. The other patient, Mrs E.P., 39 years old, who visited me on August 25, 1969, who visited me on August 25, 1969, had advanced pyelitis of the left kidney, beginning with osteosclerotic changes in the pubic bones, and exostosis at the sternum, accompanied by the same clinical picture as in the patient just discussed. The function of the diseased kidney and the other symptoms improved markedly within six weeks after she stopped drinking the municipal water in Midland, Michigan (fluoridated since January 1946). Twenty-four hour urinary fluoride excretions before and after the tests were 2.39 and 4.20 mg, respectively. For most of her life she had resided in Lubbock, Texas (water supply fluoride then 4.4 ppm). The development of osteosclerosis in this case was not surprising, since - as recorded in fluoridated Evanston, Illinois, and also in a fluoridated Finnish community - kidney patients retain as much as 60% more fluoride than do persons in normal health. In the Finnish work blood fluoride levels were 3 to 4 times higher than normal in the patients with renal disorders."

SOURCE: Waldbott GL, et al. (1978). Fluoridation: The Great Dilemma. Coronado Press, Inc., Lawrence, Kansas. pp. 155-156.

44. "Evidence of chronic fluoride intoxication, associated with renal tubular dysfunction in the group of FMBD patients, brings to focus the possibility that fluoride toxicity may be responsible for both bone and kidney disease in FMBD... Evidence is available in the literature to support our observation of fluoride-induced renal damage."
SOURCE: Harinarayan CV, et al. (2006). Fluorotoxic metabolic bone disease: an osteo-renal syndrome caused by excess fluoride ingestion in the tropics. Bone 39: 907-14.

45. "Renal function especially glomerular filtration rate was very sensitive to fluoride exposure. Inorganic phosphate concentrations in urine were significantly lower in the residents in fluorosis areas in China than in non-fluorosis area in China and Japan.... The results show that exposure to excess fluoride has caused dental/skeletal fluorosis and reduced glomerular filtration rate in the residents living in fluorosis areas.."
SOURCE: Ando M, et al. (2001). Health effects of fluoride pollution caused by coal burning. Science of the Total Environment 271(1-3):107-16.

46. "We report a case of fluoride intoxication related to potomania of Vichy water, a highly mineralized water containing 8.5 mg/L of fluoride. Features of fluoride osteosclerosis were prominent and end-stage renal failure was present. The young age of the patient, the long duration of high fluoride intake, and the absence of other cause of renal insufficiency suggest a causal relationship between fluoride intoxication and renal failure."
SOURCE: Lantz O, et al. (1987). Fluoride-induced chronic renal failure. American Journal of Kidney Disorders 10(2):136-9.

47. "Kidney damage (1) in distal and proximal tubular function, (2) in glomerular filtration, occurred in 40 to 60 year olds residing in El Quel an endemic fluorosis area in Southern Algeria compared to normals from Algiers. Functional renal disturbances are proportional to the degree of fluoride accumulation which incrases in relation to: a) the level of fluoride in drinking water, b) the fluoride level in nails and c) the radiological grade (O I II III) of fluorosis."
SOURCE: Reggabi M, et al. (1984). Renal function in residents of an endemic fluorosis area in southern Algeria. Fluoride 17: 35-41.

48. "Complete urine examinations including urea, creatinine and fluoride clearances were carried out on 25 cases of endemic fluorosis... In 10 healthy nonfluorotic subjects urea, creatinine and fluoride clearances were measured simultaneously as a control. The following results were obtained: The mean values for maximum urea clearance and standard urea clearance were low compared to mean control values. The decline in creatinine and fluoride clearances compared to the controls was statistically significant, an indication that chronic fluoride intoxication leads to a distinct impairment of glomerular function in human beings."
SOURCE: Jolly SS, et al. (1980). Kidney changes and kidney stones in endemic fluorosis. Fluoride 13: 10-16.

49. "The kidney function of 25 radiologically proven cases of endemic fluorosis was studied at the Medical College of Patiala. Evidence of statistically significant decrease in creatinine clearance is presented. Some structural abnormalities in kidneys have been

described. No significant tubular abnormalities could be demonstrated by water loading and water deprivation tests."
SOURCE: Singla VP, et al. (1976). The kidneys. Fluoride 9: 33-35.

50. "The question is whether the chronic excessive fluoride intake caused the renal damage (either directly or indirectly) or whether the systemic fluorosis was due to impaired renal function."
SOURCE: Juncos LI, Donadio JV Jr. (1972). Renal failure and fluorosis. Journal of the American Medical Association 222(7):783-5.

51. "The distribution of findings suggestive of not-normal genitourinary conditions was approximately the same for the fluoride-exposed group and the control group except for the incidence of albuminuria which was found to be higher in the exposed group. This finding and its distribution in the subgroups suggest the possibility of a relationship between fluoride exposure and increased excretion of albumin in the urine."
SOURCE: Derryberry OM, et al. (1963). Fluoride exposure and worker health. Archives of Environmental Health 6: 503-511.

52. "There is evidence from animal experiments that fluoride in large amounts causes gross alterations of renal structure and decreased tubular function. Injury with necrosis of the columnar cells lining the proximal convoluted tubules is the primary lesion... Kidney function tests were done in 28 of our cases. Blood urea ranged from 15 to 20 mg/100 ml with an average of 33. Urea clearance was done in only six cases and showed impaired function in five. The ratio of the concentration of inorganic phosphorous excreted in the urine to that in the serum is approximately 50 in normal subjects. This value increases with renal insufficiency. It averaged 67 in our cases. We found significant aminoaciduria in 4 cases. The concentration and dilution tests were essentially normal. Other kidney function tests were not done, but the existence of aminoaciduria, slightly increased blood urea, impairment of urea clearance, and a high phosphorus ratio as described all suggest a subtle disturbance of kidney function which needs further elaboration."
SOURCE: Singh A, et al. (1963). Endemic fluorosis. Epidemiological, clinical and biochemical study of chronic fluoride intoxication in Punjab. Medicine 42: 229-246.

53. "Of the 19 patients in the series, 12 were examined for the presence of albuminuria, and this was found to be present in 11. The urinary excretion of fluorine damages the kidney, which results in the common finding of albuminuria... Renal damage does appear to be a frequent occurrence and is probably due to the excretion of fluorine, analagous to renal damage caused by heavy metals."
SOURCE: Kumar SP, Harper RA. (1963). Fluorosis in Aden. British Journal of Radiology 36: 497-502.

54. "Urea Clearance Test: This test (Van Slyke method) was performed in fourteen cases... The results showed marked impairment of renal function. The mean figures for the maximum and standard clearance were 26.24 and 39.67% of the normal respectively."
SOURCE: Siddiqui AH. (1955). Fluorosis in Nalgonda district, Hyderabad-Deccan. British Medical Journal ii (Dec 10): 1408-1413.

55. "Osteosclerosis may be a dangerous sequel to the chronic ingestion of fluorine-containing water supplies, since it may give rise to a secondary anemia due to encroachment upon the blood-forming marrow. There is also the possibility of kidney damage due to chronic fluoremia."
SOURCE: Linsman JF, McMurray CA. (1943). Fluoride osteosclerosis from drinking water. Radiology 40: 474-484.

56. "Renal function was tested by determination of the filtration rate, blood urea clearance, uric acid clearance, and chloride clearance. (a) Filtration rate - ... In six cases, the filtration rate was below the normal lower limit and in three cases was within normal limits or above. (b) Blood urea clearance - This was estimated by van Slyke's method. In all the cases the figures were below the normal lower limit and in some very much below the limit. The filtration rate and blood urea clearance values show that, in the majority of the cases, kidney function is impaired, in some markedly so."
SOURCE: Shortt HE, et al. (1937). Endemic fluorosis in the Madras presidency. Indian Journal of Medical Research 25: 553-568.

57. "In the 1960s, the widespread use of the inhalational anaesthetic methoxyflurane was associated with a significant occurrence of postoperative renal dysfunction. This was attributed to hepatic biotransformation of methoxyflurane and subsequent release of inorganic fluoride ions into the circulation. Based upon the clinical experience with methoxyflurane, serum fluoride concentrations exceeding 50 mumol/l were considered to be nephrotoxic."
SOURCE: Nuscheler M, et al. (1996). [Fluoride-induced nephrotoxicity: fact or fiction?]. Anaesthesist 45 Suppl 1:S32-40.

58. "Evidence for fluoride nephrotoxicity has accumulated largely from the adverse effects of halogenated anesthetics on renal function."
SOURCE: Partanen S. (2002). Inhibition of human renal acid phosphatases by nephrotoxic micromolar concentrations of fluoride. Experimental and Toxicologic Pathology 54(3):231-7.

59. "The predominant factors in the production of methoxyflurane nephrotoxicity appear to be high methoxyflurane dosage and serum inorganic fluoride concentration."
SOURCE: Mazze RI. (1976). Methoxyflurane nephropathy. Environmental Health Perspectives 15:111-9.

60. "Kidney damage can appear within a few days following methoxyflurane anesthesia. This phenomenon was studied by Cousins and Mazze (1973), who reported that peak (i.e. transient) post-anesthesia plasma F- levels in afflicted humans exceeded 90 umol/l. The nephrotoxicity was accompanied by an increased urine volume of low osmolarity, and increased thirst, with the syndrome tending to obey a short-term dose-response pattern in man. Mazze et al. (1972) and Cousins et al. (1974) have shown that kidney damage in rats exposed to methoxyflurane was caused by high inorganic fluoride concentrations and not by oxalic acid, which is also a metabolic breakdown product of methoxyflurane. Taves et al. (1972) also related the nephrotoxicity and polyuria to the metabolically released inorganic fluoride."
SOURCE: Marier J, Rose D. (1977). Environmental Fluoride. National Research Council of Canada. Associate Committe on Scientific Criteria for Environmental Quality. NRCC No. 16081.

61. "In the kidney, glomerular hypercellularity and mesangial proliferation was apparent in animals from both the NaF and AlF3 treatment groups. Congruent with the glomerular changes was deposition of protein in the tubules. There was a significant increase in the extent of monocyte infiltration in the animals treated with with AlF3 compared to controls... Histological evidence of glomerular distortions and other signs of kidney disorders were found in animals in both the AlF3 and NaF groups, although expressed differently. It is possible that physiological alterations in kidney function, not related to histological evidence of injury, were greater in the AlF3 group than the NaF group. The overall Al content of the kidneys in the AlF3 group was nearly double that found in the NaF and control groups. Since the kidney is critical to the elimination of both Na and Al, such alterations may have influenced the body burden of these elements, detoxification in general, as well as homeostasis of a variety of important ions, such as calcium."
SOURCE: Varner JA, et al. (1998). Chronic administration of aluminum-fluoride and sodium-fluoride to rats in drinking water: Alterations in neuronal and cerebrovascular integrity. Brain Research 784: 284-298.

62. "The mean kidney enzyme activity rate was measured at 0.3863 for the control animals. In studies on experimental animals a marked reduction in kidney enzyme activity was noted in the 1 ppm group; it was measured at 0.2016 showing 47.8% decrease over the normal. Animals in the 5, 10, and 100 ppm groups showed no further ostensible inhibition in activity rate."
SOURCE: Sullivan WD. (1969). The in vitro and in vivo effects of fluoride on succinic dehydrogenase activity. Fluoride 2:168-175.

63. "No gross lesions were found in the kidneys. Microscopic examinations were made on the kidneys from 6 animals which had not received fluoride in the drinking water, on 3 receiving 1 ppm, on 1 receiving 5 ppm, and on 6 receiving 10 ppm. Interstitial nephritis was observed in all the animals examined histologically, and the severity increased in proportion to the level of the sodium fluoride in the drinking water. Renal tubule hypertrophy and hyperplasia were found in those animals receiving sodium fluoride in the water but not in the 6 rats which had not been given sodium fluoride supplementation."
SOURCE: Ramseyer WF, et al. (1957). Effect of sodium fluoride administration on body changes in old rats. Journal of Gerontology 12: 14-19.

64. "[K]idneys of animals drinking water with containing 5 ppm fluoride showed certain cytochemical characteristics which may be interpreted in terms of deleterious metabolic effects in the kidneys, which excrete most of the fluorides from the organism. This is in agreement with some earlier reported observations that kidneys, more than other organs of the body, begin to show microscopic changes after prolonged daily ingestion levels of fluoride which may produce few gross changes other than fluoride storage in bones and teeth. Ogilvie (1948) showed that a dose of 7.5 mg of sodium fluoride given intraperitoneally each day for 100 days to rats produced morphological changes in the kidneys which included oedema in the interstitial connective tissue and increased vascularity of the glomeruli and medulla. These observations suggest that fluoride compounds cannot be treated as totally harmless when administered over long periods of time in relatively small concentrations... It is believed that the increased thirst and polyyuria observed in fluoridated animals is a result of functional changes in the kidneys... Our studies show a significant change in the activity of succinate dehydrogenase in the kidneys of the animals maintained on higher levels of fluoride in the drinking water."

SOURCE: Manocha SL, et al. (1975). Cytochemical response of kidney, liver and nervous system to fluoride ions in drinking water. Histochemical Journal 7: 343-355.

65. "Our study provides the first evidence that one of the effects of long-term F exposure is a change in expression of the plasma membrane and endoplasmic reticulum Ca++ pumps in the kidney. In summary, we provided rats with fluoride in their drinking water, which produced graded, plasma fluoride concentrations that occur in humans. Our studies showed that chronic high fluoride ingestion decreases the rate of Ca++ transport across renal tubule endoplasmic reticulum and plasma membranes, and reduced the amount of ER and PM Ca++ pump protein present in the kidney membranes. We conclude that chronic high fluoride ingestion may decrease the expression, increase the breakdown, or increase the rate of turnover of plasma membrane and endoplasmic reticulum Ca++ pump proteins and possibly other enzymes as well. The observed decreases in the rate of Ca++ transport and associated decreases in plasma membrane and endoplasmic reticulum Ca++ pump expression could affect in vivo Ca++ homeostasis."
SOURCE: Borke JL, Whitford GM. (1999). Chronic fluoride ingestion decreases 45Ca uptake by rat kidney membranes. Journal of Nutrition 129:1209-13.

66. "These results demonstrate that NaF induces the process of apoptosis in renal tubules via activation of the Bax expression and Bcl-2 suppression and this action is dose dependent; thus, apoptosis plays some role in the kidney injury induced by fluoride. Our data also suggest that OPN probably acts in a protective role against apoptosis in fluoride-treated renal cells."
SOURCE: Xu H, et al. (2006). Effect of sodium fluoride on the expression of bcl-2 family and osteopontin in rat renal tubular cells. Biological Trace Element Research 109:55-60.

67. "An experiment was carried out on Sprague-Dawley rats (adult males) that for 50 days were administered, in the drinking water, NaF and NaF with caffeine (doses, respectively: 4.9 mg of NaF/kg body mass/24 h and 3 mg of caffeine/kg body mass/24 h). Disturbances were noted in the functioning of kidneys, which were particularly noticeable after the administration of NaF with caffeine. Changes in the functioning of kidneys were also confirmed by such parameters as the level of creatinine, urea, protein, and calcium. Modifications of the enzymatic antioxidative system (superoxide dismutase, catalase, and glutathione peroxidase) and lipid peroxidation (malondialdehyde) were also observed. Changes in the contents of the above parameters as well as pathomorphological examinations suggest increased diuresis, resulting in dehydration of the rats examined."
SOURCE: Birkner E, et al. (2006). Influence of Sodium Fluoride and Caffeine on the Kidney Function and Free-Radical Processes in that Organ in Adult Rats. Biological Trace Element Research 109:35-48.

68. "This experiment was designed to investigate the lipid peroxidation and histological effects of chronic fluorosis on first- and second-generation rat kidney tissues... Hydropic epithelial cell degenerations and moderate tubular dilatation were observed in some proximal and distal tubules. There were markedly focal mononuclear cell infiltrations and hemorrhage at some areas of the interstitium, especially at the corticomedullar junction. Mononuclear cell infiltrations were also evident in some peritubular and perivascular areas. Most of the vascular structures were congestive. Many Bowman capsules were narrowed. The severe degenerative changes in most of the shrunken glomerules and vascular congestion were also observed."

SOURCE: Karaoz E, et al. (2004). Effect of chronic fluorosis on lipid peroxidation and histology of kidney tissues in first- and second-generation rats. Biological Trace Element Research 102:199-208.

69. "Some halogenated agents, especially methoxyflurane, because of a higher level of fluoride production, induce a renal concentrating defect that could be related to an ascending limb impairment. We investigated the mechanisms of fluoride toxicity on an immortalized cell line... The results suggest that the Na-K-ATPase pump is a major target for fluoride toxicity in Henle's loop."
SOURCE: Cittanova ML, et al. (2002). Fluoride ion toxicity in rabbit kidney thick ascending limb cells. European Journal of Anaesthesiology 19(5):341-9.

70. "The purpose of this study was to assess renal damage in experimental fluorosis. Young albino rabbits were injected with 5, 10, 20, and 50 mg NaF/kg body weight/day for fifteen weeks and then sacrificed. No significant clinical signs of toxicity were found in animals exposed to the lowest dose. At the higher doses, however, the cytoachitecture of the kidneys exhibited increasing amounts of cloudy swellings, degeneration of tubular epithelia, tissue necrosis, extensive vacuolization in renal tubules, hypertrophy and atrophy of glomeruli, exudation, interstitial oedema, and interstitial nephritis. These changes in the kidneys result in impaired renal function in chronic fluoride intoxication."
SOURCE: Shashi A, et al. (2002). Toxic effects of fluoride on rabbit kidney. Fluoride 35: 38-50.

71. "Fluoride nephropathy was exhibited as decreased fluoride excretion and appearance of urinary B2 microglobulin."
SOURCE: Cao J, et al. (2001). Prevention of brick teas fluorosis in rats with low-fluoride brick tea on laboratory observation. Food & Chemical Toxicology 39: 615-619.

72. "The toxicokinetics of F were studied by analyzing plasma concentration of F after intravenous injection of 2.86, 5.71 and 8.57 mg/kg into male Wistar rats. A dose-response relationship was recognized between these F doses and renal tissue injury."
SOURCE: Dote T, et al. (2000). Toxicokinetics of intravenous fluoride in rats with renal damage caused by high-dose fluoride exposure. International Archives of Occupational and Environmental Health 73 Suppl:S90-2.

73. "Results showed that the total phospholipid content significantly decreased in the kidney of the rats treated with high doses of fluoride and the main species influenced were phosphatidylethanolamine (PE) and phosphatidylcholine (PC). Decreased proportions of polyunsaturated fatty acids were observed in PE and PC in kidney of fluoride-treated animals compared to controls. No changes could be detected in the amounts of cholesterol and dolichol in kidneys between the rats treated with fluoride and controls. A significant decrease of ubiquinone in rat kidney was observed in the groups treated with excessive fluoride. High levels of lipid peroxidation were detected in kidney of the rats with fluorosis. It is plausible that the specific modification of lipid composition results from lipid peroxidation. The oxidative stress and modification of cellular membrane lipids may be involved in the pathogenesis of chronic fluorosis and provide a possible explanation for the gross system damage observed in the body, especially in soft tissues and organs."
SOURCE: Guan ZZ, et al. (2000). Changed cellular membrane lipid composition and lipid peroxidation of kidney in rats with chronic fluorosis. Archives of Toxicology 74:602-8.

74. "Wistar rats were provided with distilled water containing NaF(100 mg/L), and were administered through gavage with Na2SeO3[0.1 mg/(kgBW.d)] and/or ZnSO4[14.8 mg/(kg BW.d)]. The results of biochemical, pathological and ultrastructural examinations showed that fluoride could cause serious renal impairments. The major damage induced by fluoride was epithelia of proximal renal tubules. The lipid peroxidation might be one of the mechanisms of fluoride toxicity. Na2SeO3 and ZnSO4 could antagonize the renal impairments induced by fluoride through their antioxidation. The cooperative effect of Na2SeO3 and ZnSO4 was more powerful than either Na2SeO3 or ZnSO4 alone."
SOURCE: Xue C, et al. (2000). [Study on antagonistic effects of selenium and zinc on the renal impairments induced by fluoride in rats] Wei Sheng Yan Jiu 29(1):21-3.

75. "In kidney, focal intertubular mononuclear cell infiltration was observed even at the 79 ppm level. Besides, at 132 ppm, atrophied glomeruli with more periglomerula space were noticed. More pronounced changes like periglomerular fibrosis and tubular nephrosis were observed at 191 ppm F level."
SOURCE: Kapoor V, et al. (1993). Effect of dietary fluorine on histopathological changes in calves. Fluoride 26: 105-100.

76. "At the higher dose (84 ppm in water), fluoride produced polyuria, polydipsia, and weight loss. Previous studies showed that fluoride is nephrotoxic and produces polyuria and polydipsia in the rat."
SOURCE: Turner RT, et al. (1989). The effects of fluoride on bone and implant histomorphometry in growing rats. Journal of Bone and Mineral Research 4: 477-484.

77. "The effects of chronic fluoride excess in the mouse were studied by means of polarizing microscopy in combination with a special staining technique employing Sirius red F3B, a dye which renders collagen fibrils sharply visible. It was observed that changes occur in three renal areas: the interstitium, the intrinsic vasculature and Bowman's capsule. The collagen content of each area increases after about 100 days of the total fluoride exposure... Although Bowman's capsule was thickened, the glomerular tufts and the nephrons showed edematous swelling and degeneration. A concept is developed to illustrate how early inflammatory response to the chemical effects of fluoride excess leads to vascular injury, parenchymal ischemia and fibrosis."
SOURCE: Greenberg SR. (1986). Response of the renal supporting tissues to chronic fluoride exposure as revealed by a special technique. Urologia Internationalis 41(2):91-4.

78. "marked renal toxicity was observed in postweaning rats treated on Day 29. The NaF exposure resulted in increased kidney weight and kidney/body weight ratio, profound diuresis, decreased urinary osmolality, and decreased ability to concentrate urine during water deprivation. Urinary chloride excretion was decreased for the first 2 days after NaF exposure, then increased in water-deprived rats 120 hr after treatment. Glucosuria and hematuria were present for 2 days after treatment with 48 mg/kg. Histological lesions were apparent in the proximal tubules of the treated Day 29 rats. Thus, the kidney of the suckling rat is largely unresponsive to NaF toxicity. Renal sensitivity increases abruptly after weaning in the Day 29 rat."
SOURCE: Daston GP, et al. (1985). Toxicity of sodium fluoride to the postnatally developing rat kidney. Environmental Research 37:461-74.

79. "Dose related congestion of the duodenum, liver, kidney, and lung was observed in all animals. For the two higher doses, kidney degeneration and tubular necrosis were associated with glomerular inflammation. Serum fluoride had a dose related increase, while serum calcium and glucose concentrations showed initial dose dependent decreases. Diuresis was increased for the two higher doses on day 3 or 4 following treatment.. The authors conclude that acute fluoride poisoning in sheep induces severe disturbances of kidney and liver function as reflected by the altered activity of many enzymes."
SOURCE: Kessabi M, et al. (1985). Experimental acute sodium fluoride poisoning in sheep: Renal, hepatic, and metabolic effects. Fundamentals of Applied Toxicology 7: 93-105.

80. "Activities of various enzymes were determined biochemically and histochemically in the liver and kidney of rats subjected for 10 mo. to fluoride (F-) concentrations of 0 (control), 10 (group 1) and 25 ppm (group 2) in drinking water. The activity of alkaline phosphatase, acid phosphatase and succinic dehydrogenase decreased. ATPase activity increased in liver and kidney of group 2 (25 ppm) animals. Lactic dehydrogenase activity also decreased but only in the kidney histochemically. Alterations in enzyme activities were pronounced in proximal and distal convoluted tubules of the kidney... F- interfered with intracellular metabolism in liver and kidney."
SOURCE: Singh M, Kanwar KS. (1981). Effect of fluoride on tissue enzyme activities in rat: Biochemical and histochemical studies. Fluoride 14: 132-141.

81. "Effects in the kidneys are of the first to be seen in fluoride exposure of mammals. The reason for this is considered to be the relative high concentrations of fluoride found in the kidneys and in the urine during exposure."
SOURCE: Hongslo CF, Hongslo JK, Holland RI. (1980). Fluoride sensitivity of cells from different organs. Acta Pharmacologica et Toxicologica 46:73-77..

82. "The present study assesses the effect of sodium fluoride administration on kidneys of mice. One hundred adult male Albino mice were fed 10 ppm (Group A), 500 ppm (Group B), and 1000 ppm (Group C) of sodium fluoride for 3 months... The most consistent changes in the kidneys were cloudy swelling of the tubular cells. In the highest dosage groups (B and C), sacrificed at the end of three months, we found marked necrosis of tubular cells, atrophy of the glomeruli, and areas of interstitial infiltration of round cells. It is concluded that kidneys are adversely affected by prolonged use of sodium fluoride."
SOURCE: Kour K, Singh J. (1980). Histological findings in kidneys of mice following sodium fluoride administration. Fluoride 13: 163-167.

83. "In summary, Fischer 344 rats pretreated with NaF or anesthetized with methoxyflurane showed more diuresis and natriuresis than did control animals. Urinary osmolarity was lower in the fluoride-treated group. Free water reabsorption was markedly reduced, while free water excretion was not significantly altered by pretreatment with fluoride. The results suggest that NaF and methoxyflurane alter renal function primarily by inhibiting active chloride transport in the ascending limb of Henle's loop."
SOURCE: Roman RJ, et al. (1977). Renal tubular site of action of fluoride in Fischer-344 rats. Anesthesiology 46: 260-264.

84. "In the present study, evidence was obtained which indicated a close relationship between polyuria and changes in certain urinary ion excretion in fluorosis. The maximum increase in urine volume occurred during the first day following treatment. Polyuria was accompanied by significant increases in urinary K+, Na+, Mg2+, Ca2+, and inorganic phosphate... In our experiments, mitochondrial ATPase in the kidney was found to be decreased by the dose of fluoride tested. To our knowledge, this is the first report on the *in vivo* effects of fluoride on renal (Na+ K+)-ATPase activity. The decrease in activity is apparently responsible for urinary Na+ loss and a decrease in serum Na+. In addition fluoride treatment also resulted in a significant decrease in (Ca2+ Mg2+)-ATPase activity which can be held responsible for the increase in urinary Ca2+."
SOURCE: Suketa Y, Mikami E. (1977). Changes in urinary ion excretion and related renal enzyme activities in fluoride-treated rats. Toxicology and Applied Pharmacology 40: 551-9.

85. "In the Sprague-Dawley rats, during moderate fluoride administration (120 umol/kg per day), urine osmolality and cyclic AMP excretion decreased and urine volume increased... During larger daily doses of fluoride (240 umol/kg per day) urinary osmolality and cyclic AMP decreased and volume increased, which was similar to the changes seen during lower fluoride dosages, but these parameters did not change after exogenous vasopressin."
SOURCE: Wallin JD, Kaplan RA. (1977). Effect of sodium fluoride on concentrating and diluting ability in the rat. American Journal of Physiology 232: F335-40.

86. "Frascino et al (1970, 1972) studied the effects of inorganic fluoride on the renal concentration mechanisms in dogs. The high blood fluoride levels interfere with both the generation of maximally concentrated urine and tubular free water reabsorption."
SOURCE: Gottlieb LS, Trey C. (1974). The effects of fluorinated anesthetics on the liver and kidneys. Annual Review of Medicine 25: 411-429.

87. "Supplemental fluoride lowered both the urinary calcium and phosphorus concentrations. The lowering of urinary calcium concentration was due to a dilution of excreted calcium by a fluoride-induced polyuria, since dietary sodium fluoride did not reduce the urinary calcium excretion (% of intake)... The polyuria induced by fluoride was accompanied by an enhanced sodium excretion and a decrease in osmolality. These results were consistent with previous findings that the administration of fluoride caused polyuria in laboratory animals. Further, the renal sodium gradient was markedly reduced in the fluoride-induced diuretic rat."
SOURCE: Hamuro Y. (1972). Relationship between prevention of renal calcification by fluoride and fluoride-induced diuresis and reduction of urinary phosphorus excretion in magnesium-deficient KK mice. Journal of Nutrition 102: 893-900.

88. "The present findings indicate that 50 uM plasma fluoride results in a definite increase in rate of urine flow and are consistent with the estimate made from the experience of Goldemberg in humans. The present findings also agree with the data from 3 patients who had received methoxyflurane anesthesia. Two of these patients had inorganic serum fluoride concentrations of 20 to 30 uM and no obvious diuresis; whereas the patient with a concentration of 275 uM had marked polyuria. The agreement lends further weight to the suggestion that metabolism of methoxyflurane to inorganic fluoride is a major factor in the nephrotoxicity noted after anesthesia with methoxyflurane."
SOURCE: Whitford GM, Taves DR. (1971). Fluoride-induced diuresis: Plasma concentrations in the rat. Proceedings of the Society for Experimental Biology and Medicine 137:458-460.

89. "the kidneys were abnormal in most of the animals given fluorides, with the most severe changes associated with the highest doses and longest survival periods. In addition to the previously well-known dilatation of the renal loops and ducts, PAS-positive casts were seen in pronounced cases in many dilated ducts and also typical granlulomas in the medullo-cortical zone and occasionally in the outer part of the cortex."
SOURCE: Poulson H, Ericcson Y. (1965). Chronic toxicity of dietary sodium monofluorophosphate in growing rats, with special reference to kidney changes. Acta pathologica et microbiologica Scandinavica 65: 493-504.

90. "The renal lesions seen in rats ingesting 200-500 ppm fluoride in the water for 5 days were: (1) necrosis of the tubular cells, and (2) a dilatation of the tubules especially in the corticomedullary region. Neither lesion occurred in all the rats examined; necrosis was seen more often than tubular dilatation. The tubular dilatation was similar to the lesion seen in a few rats after single, large doses of sodium fluoride (Taylor et al., 1961) and to the lesion described by Pindborg (1957) after feeding 0.05% sodium fluoride in the diet for 21-28 days... The ingestion of fluoride levels of 1-50 ppm for 6 months did not produce renal lesions in the rat. A level of 100 ppm fluoride for this period of time caused dilatation of the renal tubules in two of 12 rats."
SOURCE: Taylor JM, et al. (1961). Toxic effects of fluoride on the rat kidney. II. Chronic effects. Toxicology and Applied Pharmacology 3:290-314.

91. "All animals in group 2, which received the fluoride throughout the entire experimental period, revealed kidney changes histologically typical of chronic fluoride intoxication... The sequence of the changes in the "fluorosed kidney" is dilation of the Henle loops, followed by dilation of the convoluted tubules and later by inflammation. During the recovery process the dilation disappeared first, followed by a slower reduction of inflammation. As would be expected the amount of fibrosis was unchanged. Finally, it should be mentioned that a year after the cessation of excessive fluoride diet a minority of rats still had dilated Henle loops and convoluted tubules. In these cases the interstitial inflammation and fibrosis were most pronounced. It remains for future research to establish how much fluoride it is possible to give rats without creating irreversible kidney changes."
SOURCE: Lindemann G, et al. (1959). Recovery of the rat kidney in fluorosis. Archives of Pathology 67: 30-33.

92. "Two hundred and twenty-six white rats were given a diet containing 0.05 per cent sodium fluoride (226 ppm) for periods ranging from 3 to 56 days. It was established that changes in the kidneys occured regularly after 21-28 days on the diet... The kidney changes consisted primarily in dilatation of the Henle loops in the juxtacortical area of the medulla, soon followed by a flattening of the epithelium in the convoluted tubules in the cortex and a distention of the tubules, possibly due to some kind of 'stop' in the Henle loops."
SOURCE: Pindborg JJ. (1957). The effect of 0.05 per cent dietary sodium fluoride on the rat kidney. Acta pharmacolgica et toxicologica 13: 36-45.

93. 'In previous papers, the author reported impairment of renal function due to fluorosis. The current study presents morphological renal changes of rabbits and young albino rats due to fluorosis... On gross examination, no marked changes were observed. However, in both groups which had been given 30 and 50 mg of NaF per kg of body weight, inflammatory

changes in the glomeruli with increased cellularity, capillary hyperemia, exudation, hypertrophy or atrophy, tubular degeneration with cloudy swelling, vascular degeneration and protein casts or blood in the tubular lumens were seen microscopically... The above-mentioned morphological changes, combined with impairment of renal function described in the previous reports, indicate that fluoride causes serious damage to kidneys."
SOURCE: Kawahara H. (1956). Experimental studies on the changes of the kidney due to fluorosis. Part III. Morphological studies on the changes of the kidney of rabbits and growing albino rats due to sodium fluoride. Shikoku Acta Medica 8:283-28. (Abstracted in: Fluoride 1972; 5:50-53.)

94. "In previous papers the author reported disturbances of renal function, especially changes in the urine, serum NPN, serum creatinine and serum chlornatrium of rabbits due to ingestion of fluoride. The current investigation deals with the effect of sodium fluoride on renal clearance, particularly on plasma urea clearance, on renal plasma flow (RPF) and glomerular filtration rate (GFR) in rabbits... The authors concluded from the experimental data presented here that the administration of fluoride in the above doses impairs the kidney function."
SOURCE: Kawahara H. (1956). Experimental studies on the changes of the kidney due to fluorosis. Part II. Influence of sodium fluoride on renal clearance in rabbits. Shikoku Acta Medica 8:273-282. (Abstracted in: Fluoride 1972; 5:48-50.)

95. "The following experiments were conducted in order to determine possible renal changes by fluoride. Mature male rabbits weighing over 1.5 kg were given orally 1%, 3%, 5% sodium fluoride solutions which provided 10, 30 and 50 mg respectively of sodium fluoride per kg body weight... The above results or urine and blood suggest that renal damage occurs in fluorosis."
SOURCE: Kawahara H. (1956). Experimental studies on the changes of the kidney due to fluorosis. Part I: Influence of sodium fluoride on the urine changes and non-protein nitrogen, creatinine and sodium chloride in serum of rabbits. Shikoku Acta Medica 8:266-272. (Abstracted in: Fluoride 1972; 5:46-48.)

96. "Rats given small amounts of NaF in the diet exhibited, in addition to the well-known skeletal and dental fluorosis, marked polydipsia and polyuria... The histological examination indicated that in the kidneys there was a vascular, glomerular and more obviously tubular degeneration leading finally to interstitial fibrosis."
SOURCE: Bond AM, Murray MM. (1952). Kidney function and structure in chronic fluorosis. British Journal of Experimental Pathology 33: 168-176.

97. "The only organ found to be changed macroscopically was the kidney... The kidneys all had the same appearance, being contracted and paler in colour than normally; the surface was irregular, in most cases granulated. Only some of the rats displayed macroscopic kidney changes of this kind... Under the microscope the kidneys of Rats 4,5,6,10,11,21,22,25 all showed signs of a chronic, mostly interstitial nephritis of uniform character; the changes were slight in Rats 5 and 6, which had not shown macroscopic changes, pronounced in the others... The changes in the kidney of Rat 21 are described below as being typical: The kidney is contracted, the surface very uneven. The changes are diffusely spread. Many glomeruli show serous or hyaline degeneration. The lumina of tubuli in most cases are irregularly dilated; this often forms cystic areas with an abundant serous content. Epithelium in the tubuli is low but well preserved. Universally there is proliferous development of connective tissue; the tissue is

hyperaemic and contains scattered round-cell infiltration. A slight calcification in the tissue is observed in one place. Vessels normal."
SOURCE: Roholm, K. (1937). Fluorine Intoxication. London: Lewis p 219.

Fluoride/Kidney Stones - Association

"These studies indicate that ingestion of excess fluoride facilities calcium oxalate crystalluria and promotes the formation of bladder stones in rats, under the experimental conditions used."
SOURCE: Anasuya A. (1982). Role of fluoride in formation of calculi: studies on rats. Journal of Nutrition 112(9):1787-95.

"Of the elements tested, only silicon and fluoride accelerated calcium uptake, whereas magnesium had an inhibitory effect. The simultaneous presence of silicon and fluoride in the medium had a synergistic action on calcium uptake. Urine of stone formers showed high propensity to mineralize tendon collagen, but not the urine of non-stone formers. Total content, and concentration of silicon in urine of stone formers was significantly higher than in normal urine. Addition of silicon to non-stone formers urine enhanced its capacity to mineralize collagen in vitro. These results strongly suggest the possible involvement of silicon and fluoride in the genesis of urinary calculi in man."
Anasuya A, Rao BS. (1983). Effect of fluoride, silicon and magnesium on the mineralizing capacity of an inorganic medium and stone formers urine tested by a modified in-vitro method. Biochemistry and Medicine 30:146.

"The incidence of urinary tract calculi was elevated in most of the fluorotic districts in Punjab."
SOURCE: Jolly SS, et al. (1980). Kidney changes and kidney stones in endemic fluorosis. Fluoride 13(1): 10-16.

Machov P (1995) Analytical evaluation of urinary calculi mineral composition. Ann Acad Med Stetin 41:259.

Rathee N, Garg P, Pundir C.S. (2004). Correlative study of fluoride content in urine, serum and urinary calculi. Indian Journal of Clinical Biochemistry 19: 100-102.

Vahlensieck W (1985) Influence of water quality on urolithiasis. In: Schwille PO, Smith LH, Robertson WG, Vahlensieck W (eds) Urolithiasis and related research. Plenum, New York, p 97

"In conclusion, the data suggest that fluoride in vivo may behave as a mild promoter of urinary stone formation by:
(a) excretion of insoluble calcium fluoride,
(b) increasing oxalate excretion and
(c) mildly increasing the oxidative burden."
SOURCE: Singh PP, Barjatiya MK, Dhing S, Bhatnagar R, et al. (2001). Evidence suggesting that high intake of fluoride provokes nephrolithiasis in tribal populations. Urological Research 29(4): 238-44.
A significant number of these citations were assembled by Fluoride Action Network.