

Q & A 154.4

Fluoride toothpaste – what are the dangers of chronic ingestion in adults?

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Summary

- ◆ Chronic toxicity from fluoride ingestion is rare in the UK and other developed countries. The principal sources of potentially excessive fluoride intake are drinking water, in areas where levels are naturally high, and toothpaste ingestion.
- ◆ US guidance suggests that the tolerable upper limit for fluoride ingestion is 10 mg per day.
- ◆ Most public water supplies in the UK contain less than 0.7 mg/L fluoride; 10% of supplies are fluoridated to a level of 1.0 mg/L (1 part per million fluoride – ppmF).
- ◆ Standard over-the-counter adult toothpastes contain between 1,000 ppmF and 1,500 ppmF. There are two toothpastes, available only on prescription, with fluoride contents above 1,500 ppmF. They are Duraphat[®] 2800 (2,800 ppmF) and Duraphat[®] 5000 (5,000 ppmF).
- ◆ A 70 kg adult, who does not expectorate after brushing, could ingest a total of 10 mg fluoride by swallowing 2.0 ml of Duraphat[®] 5000 toothpaste, assuming a fluoride-free water supply, or 1.7 ml Duraphat[®] 5000 toothpaste plus 1.5 litres water containing 1 ppmF.
- ◆ Caution is required if high-strength fluoride toothpastes are used in people who may swallow rather than expectorate after toothbrushing.

Background

The introduction on to the UK market of two high-strength prescription-only fluoride toothpastes (Duraphat[®] 2800 and Duraphat[®] 5000) has raised questions about their safety if ingested chronically. Although the patient information provided with the toothpaste warns against swallowing, many patients who require the use of high strength fluoride toothpastes have special needs and may find spitting out the toothpaste difficult, leading to chronic ingestion. These high-strength fluoride toothpastes were marketed following publication of an increasing body of evidence that fluoride exerts its effect on dental caries due to its topical application whether via fluoridated water, fluoride drops/tablets, fluoridated salt, fluoridated milk etc. or, more commonly in the UK, via toothbrushing. Previously fluoride was primarily thought to be incorporated into developing tooth enamel following systemic absorption [1,2]. The dangers of dental enamel fluorosis after excessive ingestion of fluoride in children under 7 years are well documented and not covered in this Q&A.

Ingestion of large amounts of fluoride acutely is well recognised to cause severe and potentially fatal adverse effects; the signs, symptoms and management of acute fluoride toxicity are addressed by the National Poisons Information Service Toxbase database (www.toxbase.org, registration required).

This Q&A examines the effects of chronic fluoride ingestion associated with use of fluoride toothpaste in adults.

Answer

How much fluoride is there in toothpaste?

The maximum amount of fluoride allowed in toothpaste, by UK and EC law, for use as an oral hygiene product before it is classified as a medicine, is 0.15% [3,4]. This is equivalent to 1,500 parts per million fluoride (ppmF). The main fluorides found in toothpaste are sodium fluoride, sodium mono-

Q&A 154.4 Fluoride toothpaste – what are the dangers of chronic ingestion in adults?

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fluorophosphate and stannous fluoride. Many toothpaste packs express fluoride content as a percentage of the active fluoride salt. Table 1 shows approximate equivalence between fluoride content expressed as mg per ml, ppmF and as a percentage. The amount of fluoride found in over-the-counter adult toothpaste ranges from 1,000 to 1,500 ppmF.

Table 1 Comparison of fluoride content in adult toothpaste

ppmF	Fluoride mg/ml	Sodium Fluoride	Sodium Mono-fluorophosphate	Stannous fluoride
5,000	5	1.1%	3.8%	2.1%
2,800	2.8	0.619%	2.13%	1.18%
1,500	1.5	0.32%	1.14%	0.63%
1,450	1.45	0.32%	1.1%	0.61%
1,100	1.1	0.24%	0.84%	0.454%
1,000	1	0.22%	0.76%	0.4%

Fluoride content of water and food

The regulatory limit for fluoride in the UK public water supply, defined by *The Water Supply (Water Quality) Regulations 2010* is 1.5 mg/L [5]. Most public water supplies contain less than 0.7 mg/L fluoride. However, 10% of the UK water supply is artificially fluoridated to a level of 1.0 mg/L (1 ppmF) as a public health measure to protect against dental decay [6]. For the estimated fluoride intake from water fluoridated to 1 ppmF see Table 2.

Table 2 Estimated fluoride intake from water fluoridated to 1mg/L (1 ppmF) [6]

Age	Average body weight (kg)	Estimated average consumption of water (L/day)	Estimated fluoride intake from water (mg/kg/day)	Estimated daily fluoride intake (mg/day)
7 months to 4 years	13	0.8	0.062	0.8
5 to 11 years	27	0.9	0.033	0.9
Above 12 years	57	1.3	0.023	1.3
Adults (≥ 18 years)	70	1.5	0.021	1.5

Most foods have fluoride concentrations well below 0.05 mg/100 g. Exceptions, other than fluoridated water and drinks, include tea and some marine fish [7].

Effects of chronic fluoride ingestion in adults

Features of chronic fluoride toxicity include gastrointestinal effects (dyspepsia, nausea, diarrhoea and vomiting) and skeletal fluorosis characterised by skeletal abnormalities and joint pain, osteosclerosis (abnormal hardening of bone) and exostoses (bony outgrowths) of long bones, vertebra and jaws. Fluoride is deposited irregularly in the bones and bone can be laid down along the muscle attachments and tendons [8]. Histologically, skeletal fluorosis resembles osteomalacia (inadequate or delayed mineralisation in mature cortical and spongy bone) but biochemically the plasma calcium and phosphate levels are normal. The strength of fluorotic bone is poor and spontaneous fractures are common [9].

Chronic fluoride toxicity is related directly to the extent and duration of fluoride exposure; however, crippling skeletal fluorosis is extremely rare in the UK and other developed countries. Chronic toxicity from fluoride ingestion has been reported in association with ingestion by cryolite (compound of aluminum fluoride and sodium fluoride) workers and in geographical areas which are hot and dry and have extremely high levels of fluoride present in the water [6,8]. There is no evidence of clinical skeletal fluorosis arising from exposures to water supplies in the UK [6].

Due to its ability to increase bone mass, fluoride has been used experimentally for over 30 years as a treatment for osteoporosis at doses ranging from 9 mg to 41 mg of fluoride daily; published trials report use for up to four years [10]. However, although fluoride increases bone mineral density it does not reduce the risk of vertebral fractures and results in increased non-vertebral fractures and lower limb pain resulting from microfractures [10]. Skeletal fluorosis generally only develops if fluoride intake exceeds 10 mg daily for at least 10 years [7].

In the UK there is no maximum recommended daily amount of fluoride. However, in the US the '*Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board*' gives guidance on fluoride ingestion. The recommendation is that the tolerable upper limit for fluoride is 10 mg daily [7]. [N.B. From Table 2, a 70 kg man drinking 1.5L daily of water containing 1 ppm fluoride would ingest approximately 1.47 mg fluoride each day.]

Can toothpaste ingestion lead to fluoride toxicity?

There are three published cases of fluoride toxicity associated with toothpaste ingestion. The first case describes skeletal fluorosis associated with toothpaste ingestion in a 45-year-old woman who complained of painful swelling of the fingers [11]. Laboratory tests showed elevated fluoride levels in the blood and urine. The woman admitted to excess and unusual use of toothpaste; she brushed her teeth 18 times a day and swallowed the toothpaste, because she liked the taste. She consumed a tube of toothpaste every two days, thereby swallowing 68.5 mg of fluoride every day. The patient was asked to use toothpaste without fluoride; 16 weeks later the pain had ceased and laboratory tests showed massively reduced but still elevated fluoride levels in the blood and urine.

The second case describes a 52-year-old man with osteosclerosis and elevated fluoride levels [12]. The man presented with severe neck immobility of seven-year duration and investigation revealed skeletal fluorosis. Due to the patient's almost obsessive dental hygiene regimen, surreptitious ingestion of toothpaste was considered the most plausible fluoride source; he brushed his teeth using fluoridated toothpaste, before and after all meals (minimum six times daily) and kept a toothbrush at work. Within three months of removal of fluoride toothpaste, urine fluoride levels had dropped and were normal after nine years. Serum fluoride normalised within eight months. All arthralgias resolved within two years. After 8.5 years, bone fluoride was reduced but was still 10 times the reference value.

In the third case a 58-year-old lady presented with a fracture in her foot [13]. Radiographs showed marked osteosclerosis of the spine and pelvis. Initially fluorosis was not suspected but fluoride levels measured over two years after the initial fracture showed greatly elevated levels in the serum, bone and urine. Exploration of fluoride ingestion revealed that she had drunk approximately six cups of tea daily for the last five to ten years. During initial questioning about her use of fluoride toothpaste she described brushing her teeth three times daily and using a 100g tube of standard strength fluoride toothpaste weekly. However, subsequent discussion revealed that she brushed her teeth up to ten times daily. From her consumption of tea plus her tooth brushing routine she was estimated to be ingesting approximately 17-18mg of fluoride daily.

How much fluoride toothpaste is too much?

In the first case above the patient was ingesting 68.5 mg fluoride daily which equates to:

- 13.7 ml of Duraphat® 5000 toothpaste.
- 24.5 ml of Duraphat® 2800 toothpaste.
- 45.7 ml of 1,500 ppmF toothpaste.
- 68.5 ml of 1,000 ppmF toothpaste.

Using the US guidance of 10 mg fluoride per day as the tolerable upper daily limit, the amount of fluoride toothpaste considered safe for a 70 kg adult to ingest, allowing for ingestion of 1.5 L water either at 0 ppmF or 1 ppmF, is given in Table 3;

Table 3 Approximate safe daily limit of fluoride toothpaste ingestion for 70 kg adult

Toothpaste strength (ppmF)	Approximate safe daily volume of toothpaste ingestion (measured in mls)		Approximate safe daily volume of toothpaste ingestion (measured as toothbrush head length coverage*)	
	1.5 L water 0 ppmF (0 mg fluoride)	1.5 L water 1 ppmF (1.47 mg fluoride)	1.5 L water 0 ppmF (0 mg fluoride)	1.5 L water 1 ppmF (1.47 mg fluoride)
5,000	2	1.7	2	1.7
2,800	3.6	3.1	3.6	3.1
1,500	6.7	5.7	6.7	5.7
1,000	10	8.5	10	8.5

*standard 2.5 x 1.0 cm head, strip applied from pump dispenser along full 2.5 cm length equates to approximately one ml.

Limitations

- ◆ There are no UK recommendations for safe levels of fluoride ingestion in adults.

References

1. Opinion of the scientific committee on cosmetic products and non-food products intended for consumers. The safety of fluorine compounds in oral hygiene products for children under the age of 6 years. SCCNFP/0653/03, June 2003. (Accessed online at http://ec.europa.eu/health/ph_risk/committees/sccp/documents/out219_en.pdf on 26/10/07, 21/10/09, 2/12/11 and 31/12/13).
2. Marinho VCC, Higgins JPT, Logan S and Sheiham A. Fluoride toothpastes for preventing dental caries in children and adolescents. Cochrane Database of Systematic Reviews 2003, Issue 1. Art.No.: CD002278. DOI: 10.1002/14651858.CD002278 (Accessed online at <http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD002278/frame.html> on 26/10/07, 21/10/09, 2/12/11 and 31/12/13).
3. The Cosmetic Products (Safety) Regulations 2008 Statutory Instruments No. 1284, Schedule 4 Part 1, List of substances which cosmetics products must not contain except subject to restrictions and conditions (Accessed online at http://www.opsi.gov.uk/si/si2008/uksi_20081284_en_4#sch4 on 21/10/09, 2/12/11 and 31/12/13).
4. Regulation (EC) N° 1223/2009 of the European Parliament and of the Council on cosmetic products, Annex III – List of substances which cosmetic products must not contain except subject to the restrictions laid down. (Accessed online at <http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:342:0059:0209:EN:PDF> on 31/12/13).
5. The Water Supply (Water Quality) Regulations 2010 (Accessed online at <http://www.legislation.gov.uk/wsi/2010/994/contents/made> on 2/12/11 and 31/12/13).
6. Committee on Toxicity. COT Statement on Fluorine in the 1997 total diet study. COT statement 2003/03, September 2003 (Accessed online at <http://cot.food.gov.uk/pdfs/fluoride.pdf> on 31/12/13).
7. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board. *Dietary Reference Intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride*. Washington, DC: National Academy Press, 1997. p 288-313 (Accessed online at <http://www.nap.edu/openbook.php?isbn=0309063507> on 26/10/07, 21/10/09, 2/12/11 and 31/12/13).
8. Dollery C, editor. *Therapeutic Drugs*. Edinburgh: Churchill Livingstone; 2nd edition 1999, pF102.
9. Seymour RA, Meechan JG and Yates MS. *Pharmacology and Dental Therapeutics*. New York: Oxford University Press; 3rd edition 1999, p181.

Q&A 154.4 Fluoride toothpaste – what are the dangers of chronic ingestion in adults?

Prepared May 2014

Available at www.sps.nhs.uk

10. Haguenauer D, Robinson VA, Shea BJ, Tugwell P, Wells G. Fluoride for treating postmenopausal osteoporosis. *Cochrane Database of Systematic Reviews* 2000, Issue 4. Art. No.: CD002825. DOI: 10.1002/14651858.CD002825 (Accessed online at <http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD002825/frame.html> on 26/10/07, 20/10/09, 2/12/11 and 31/12/13).
11. Roos J, Dumolard A, Bourget S et al. Osteofluorosis caused by excess use of toothpaste. *Presse Med.* 2005; 34: 1518-20 (French, information from English abstract only).
12. Kurland ES, Schulman RC, Zerwekh JE et al. Recovery from skeletal fluorosis (an enigmatic, American case). *J Bone Miner Res* 2007; 22: 163-170.
13. Joshi S, Hlaing T, Whitford G.M. and Compston J.E. Skeletal fluorosis due to excessive tea and toothpaste consumption. *Osteoporosis International*, 2011; 22: 2557-2560.

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Search strategy

Medline (Pubmed) searched on 26/10/07, 21/10/09, 2/12/11 and 31/12/13:

("Dentifrices/adverse effects"[Mesh] OR "Dentifrices/toxicity"[Mesh] OR "Toothpastes/poisoning" [Mesh]) and "Bone Diseases/chemically induced"[MAJR] Limits: Humans, Adolescent: 13-18 years, Adult: 19-44 years, Middle Aged: 45-64 years, Middle Aged + Aged: 45+ years, Aged: 65+ years, 80 and over: 80+ years

("Fluorides/adverse effects"[Mesh]) OR ("Fluorides/toxicity"[Mesh])

("Fluorides/adverse effects"[Mesh]) OR ("Fluorides/toxicity"[Mesh]) and "Bone Diseases/chemically induced"[MAJR] Limits: Humans, Adolescent: 13-18 years, Adult: 19-44 years, Middle Aged: 45-64 years, Middle Aged + Aged: 45+ years, Aged: 65+ years, 80 and over: 80+ years.

Embase (NICE HDAS) searched on 26/10/07, 21/10/09, 2/12/11 and 31/12/13:

exp*TOOTHPASTE/ and exp*FLUOROSIS/

DRUGDEX®System: McLean W & Ariano R: Fluoride In: Klasco RK (Ed): DRUGDEX® System (electronic version). Thomson Micromedex, Greenwood Village, Colorado, USA. Available at: <http://www.thomsonhc.com/>(cited: 26/10/07, 21/10/09, 2/12/11 and 31/12/13).

NICE Evidence Search

Toothpaste and fluorosis, toothpaste (clinical), toothpaste (drug prescribing and safety)

Q&A 154.4 Fluoride toothpaste – what are the dangers of chronic ingestion in adults?

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Textbooks:

Dollery C, editor. *Therapeutic Drugs*. Edinburgh: Churchill Livingstone; 2nd edition 1999.

Seymour RA, Meehan JG and Yates MS. *Pharmacology and Dental Therapeutics*. New York: Oxford University Press; 3rd edition 1999.

Sweetman SC (ed), *Martindale: The Complete Drug Reference*. (online). London: Pharmaceutical Press; Sodium fluoride. [Accessed via www.medicinescomplete.com on 26/10/07, 21/10/09, 2/12/11 and 31/12/13].

McEvoy GK (ed) *AHFS Drug Information* (online) American Society of Health-System Pharmacists. Fluorides [Accessed via www.medicinescomplete.com 26/10/07, 21/10/09, 2/12/11 and 31/12/13].

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