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Cases Studies of Vitamin D Toxicity

TABLE G-1 Case Studies of Vitamin D Toxicity

Study	Patient/Population	Preparation; Dose	Duration
<i>Children</i>			
Djamil and Tu-Tunji. 1931. Lancet letter to the editor	2-yr-old male	Vigantol (irradiated ergosterol); 3 tsp	1 d
1947. BMJ letter to editor	Not specified	Cod liver oil	
Ross. 1952. Journal of Pediatrics :815-822	4 infants ages 8-14 mo	Irradited ergosterol containing an estimated 30,000–40,000 IU vitamin	Daily for 8-12 mo
Jacqz et al. 1985	Infants with hypercalcemia (2 cases with vitamin D toxicity) Case 1: 3 mo old Case 2: 7 mo old	Vitamin D and calcium supplementation 300 µg D ₃	
Besbas et al. 1989. Turkish J Pediatrics 31:239-244	Case 1: 3 mo old	Vitamin D: 45,000 IU/d	45 d
Dent. 1964. BMJ letter to editor	Case 2: 4 mo old	Vitamin D: 60,000 IU/d	30 d
Counts et al. 1975. Ann Internal Med 82:196-200	6 yr old	Vitamin D (Calciferol Tablets B.P.): 1.25 mg. (~50,000 IU)/d	9 mo
DeWind. 1960. Arch Dis Child 36:373-380	4-yr-old male	Vitamin D ₂ (Drisdol): 50,000 up to 100,000 IU/d	2 mo following bilateral nephrectomy
Barrueto et al. 2005. Pediatrics 116:e453-e456	5.5 yr old	Vitamin D: 100,000 IU + cod liver oil-2 T + multivitamin	daily × 2–3 mo; and continued intake of tx vitamin D for 1 yr after hospitalization
	2-yr-old male	Vitamin D (ergocalciferol): 2,400,000 IU	4 d

Serum Calcium	Serum 25(OH)D	Symptoms/Health Effects
		Edema and albuminuria
18–19 mg/dL		<p>Response from editor: A toxic dose of more than 200,000 units would only be achieved with ingestion of 2.65 L cod liver oil/d</p> <p>All presented with anorexia, weight loss, weakness; 2 infants recovered within 6–9 mo following removal of vitamin D; 2 infants died: autopsy showed fibrotic changes in vascular tissue, calcification of other tissues was noted, particularly lung</p> <p>Both cases presented with anorexia, diarrhea, and vomiting</p>
10.5 mg/dL	129 ng/ml	
10.5 mg/dL	126 ng/ml	
19.5 mg/dL		Calcium phosphate crystals in urine; bilateral medullary nephrocalcinosis; vomiting and lethargy; both pts recovered without incident
17.6 mg/dL		Extreme thirst, hypercalcemia, symptoms of diabetes insipidus
17.2 mg/dL	635 ng/ml	Leg pain, cessation of growth resulting from bone resorption; serum calcium, accompanied by nausea and vomiting. Tx with Ca-free dialysate failed to reduce serum Ca; prednisolone for 7 d; calcitonin tx stabilized serum Ca
17 mg/dL		Nausea and non-tender lumps over both tibias; X-rays showed alternating patterns of increased and decreased bone density. Loss of bone density and tissue calcification continued despite removal of vitamin D and the pt died
14.4 mg/dL	470 ng/ml	Constipation and colic; persistent hypertension; no renal, cardiac, neurological symptoms noted. Acute toxicity treated with furosemide, calcitonin, and hydrocortisol

continued

TABLE G-1 Continued

Study	Patient/Population	Preparation; Dose	Duration
<i>Adults</i>			
Puig. 1998. Ann Internal Med 128(7):601-602	66-yr-old female	Vitamin D: 200 IU + 1,000 mg calcium/twice daily	3 yr
Rizzoli et al. 1994. Bone 15:193-198	7 adults ages 55–84	Vitamin D ₃ : 30,000–60,000 IU/d	3 weeks to 7.5 yr
Davies and Adams. 1976. The Lancet	Case 1: 59-yr-old female post-thyroidectomy for 40 yr	Vitamin D: 50,000–100,000 IU/d	>30 yr
	Case 2: 71-yr-old female with Paget's disease	150,000 IU/d	7 yr
	Case 3: 51-yr-old female	100,000 IU/d	10 yr
1950. BMJ letter to editor		Vitamin D ₂ : 100,000 IU/d	3 weeks
Streck et al. 1979. Arch Intern Med 139:974-977	49-yr-old female post-thyroidectomy	Vitamin D: 100,000 units/d; plus high calcium diet	3.8 yr
Sterling and Rupp. 1967. Acta Endocrinologica 54:380-384	69-yr-old male with carcinoma of the larynx	Vitamin D (Calciferol): 100,000 units/d	3 weeks
Aub. 1951. Amer Prac 2(11):976-981	59-yr-old female	Vitamin D: 150,000 units/d	6–8 weeks
Vieth et al. 2002. Lancet 359:672	29- and 63-yr-old related males	Vitamin D poisoning: 12.6 mg D ₃ /g crystalline sugar (~1,700,000 IU/d)	7 mo

Serum Calcium	Serum 25(OH)D	Symptoms/Health Effects
4.04 mmol/L (16.2 mg/dL)	696 nmol/L (278.8 ng/ml)	Anemia and dehydration; toxicity treated with milk-free diet
3.30 mmol/L (mean) (13.2 mg/dL) (range = 2.52– 4.59 mmol/L) (10.8–18.4 mg/ dL)	710 nmol/L (mean) (284.5 ng/ml) (range = 221– 1692 nmol/L) (88.5–677.9 ng/ml)	Asthenia, anorexia, nausea, polydipsia, polyuria; hypercalciuria; PTH levels were low normal. Discontinuation of vitamin D normalized calcemia in 3 d and calcidiol levels in 3 mo; bisphosphonate was used to inhibit bone resorption
3.1 mmol/L (12.4 mg/dL)		Pts reported nausea, vomiting; case 3 had extensive arterial and ligamentous calcification; tx with corticosteroids and withdrawal of vitamin D
4.5 mmol/L (18 mg/dL)	450 nmol/L (180.3 ng/ml)	
3.75 mmol/L (15 mg/dL)	400 nmol/L (160.3 ng/ml)	Pt reported feeling well. Response from editor: Feeling well occurs early in toxicity. Toxic dose varies from 200,000–400,000 IU daily for 10 d.
12.8 mg/dL; (Urinary calcium: 493– 600 mg/24 hr)	283 ng/mL	Tx with prednisone resolved hypercalcemia via inhibition of bone resorption of calcium
3.8–5.1 mEq/L (15.2–20.4 mg/dL)		Nausea, anorexia, polyuria that progressed to dehydration and coma. Removal of vitamin D and tx with corticosteroids resolved elevated calcium and CV abnormality
14.3 mg/dL		Weight loss, memory loss; evidence of renal damage and corneal calcification. Tx not discussed
3.82 mmol/L (15.3 mg/dL)	1,555 nmol/L (623 ng/ml)	Anorexia, fever, chills, vomiting, increased thirst; 5 kg weight loss; conjunctivitis, acute renal failure, PTH <1 pmol/L. Tx with IV hydrocortisone, sodium phosphate, and pamidronic acid; both patients survived.

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TABLE G-1 Continued

Study	Patient/Population	Preparation; Dose	Duration
Lilienfeld-Toal et al. 1978. <i>Klin Wschr</i> 56:715-717	70 yr old	Vitamin D ₃ ; 15 mg/d	3 weeks
Selby et al. (1995)	6 patients (most were hypoparathyroid)	2.5–5.0 mg/d, (80,000 IU to 200,000 IU D ₂)/d	2–13 yr
Irnell (1969) <i>Acta Med Scand.</i> 185:147-152, 1969)	34-yr old	270,000 IU/d 45,000 IU/d	10 d 6 yr
<i>Accidental or Industrial Poisoning</i>			
Scanlon et al. 1995. <i>Am J Public Health</i> 85:1418-1422	234 survey respondents	Milk over-fortified with vitamin D at 70–600X concentration; (>50 IU/100 g)	Intake range: (oz/d) < 5.5 5.5–11.0 11.1–19.6 ≥ 19.7
Blank et al. 1995. <i>Am J Public Health</i> 85:656-659	Hospital discharge, lab, and health dept data from cases of hypervitaminosis D	Milk over-fortified with vitamin D + other risk factors, i.e., use supplements; sun sensitivity, history of cancer	~3 yr
Jacobus et al. 1992. <i>New Engl J Med</i> 326:1173-1177	8 individuals ages 8 mo to 82 yr consumed milk excessively fortified with vitamin D	Milk over-fortified with cholecalciferol at concentrations of 396,400 and 376,800 IU/ml	Variable exposure
Thomson and Johnson. 1986. <i>Postgrad Med J</i> 62:1025-1028	7 family members; 3 adults and 4 children ages 1.5 to 14 yr	Unknown food source containing excessively high vitamin D	Single exposure
Pettifor et al. 1995. <i>Ann Intern Med</i> 122:511-513	10 family members and 1 servant; age range 8-69 yr ingested oil containing a veterinary vitamin D concentrate	Cholecalciferol concentrate in peanut oil = 2 million U/g	Unknown exposure

Serum Calcium	Serum 25(OH)D	Symptoms/Health Effects
6.1 mval/L	498 nmol/L (200 ng/ml)	Fatigue and psychotic symptoms; no evidence of 2° osteoporosis was found. Tx with vitamin D was interrupted; the increased body pool of calcium returned to normal when serum vitamin D levels decreased to 200 ng/ml
3.26 mmol/L (mean) (13.04 mg/dL)	842 nmol/L (mean) (337.3 ng/ml)	Admitted for hypercalcemia; renal failure
6.6 mEq/L 8.5–9.6 mEq/L		Patient exhibited symptoms of toxicity (tiredness, vomiting, diarrhea, polyuria, weight loss, muscular weakness, headache) at 45,000 IU/d
mean (mg/dL)	mean (ng/ml)	Linear regression model showed a 1 oz increase in milk intake was associated with 1.39 ng/ml increase in serum 25(OH)D. No association was found between milk intake and elevated serum calcium; there was an association with elevated serum 25(OH)D and urinary calcium
2.4	32.8	
2.3	39.5	
2.4	41.3	
2.4	44.7	
13.1 mg/dL (mean for 35 cases)	224 ng/ml (mean for 35 cases)	Consumption of milk from sources other than the over-fortified milk was not associated with hypervitaminosis D
7 of 8 had hypercalcemia; 1 had hypercalcuria with normocalcemia	Mean for all cases: 731 ± 434 nmol/L (293 ± 174 ng/ml)	Vitamin D ₃ concentrate in milk that was up to 580 times in excess resulted in elevated serum vitamin D ₃ , but not D ₂ in consumers. All consumers of the milk had elevated 25(OH)D levels and most had hypercalcemia
2.72– 4.08 nmol/L (10.9–16.3 mg/dL)	832–1,287 nmol/L (333.0–515.6 ng/ml)	Serum calcium levels returned to normal within 24 d but 25(OH)D levels remained elevated for 1 yr; 1,25(OH)D was not significantly elevated in the adults
3.46–4.61 nmol/L (13.8–18.4 mg/dL)	847–1,652 nmol/L (339.3–661.9 ng/ml)	Cholecalciferol poisoning did not elevate total 1-25(OH) ₂ D in 8 and only marginally in 3 of intoxicated patients; but did elevate free 1-25(OH) ₂ D in all

continued

TABLE G-1 Continued

Study	Patient/Population	Preparation; Dose	Duration
Hodges. 1985. British Med J 290:748-749.	32-yr-old male working with crystalline vitamin D in a laboratory setting	Unknown exposure	Intermittent exposure: 32 d in 1981; 11 d in 1982; 22 d in 1983
Klontz. 2007. New Engl J Med 357:308-309	58-yr-old female diagnosed with diabetes and rheumatoid arthritis	Vitamin D ₃ overdose in a supplement; 186,906 IU/6 capsules	~2 mo
Down et al. 1979. Postgrad Med J 55:897-902	3 family members; 2 adults ages 24 yr and 1 infant aged 11 mo	Cholecalciferol concentrate in nut oil = 5 million IU/ml	Single exposure
Chiricone et al. 2003. J Nephrol 15:917-921	Case reports: 62-yr-old male 55-yr-old female	Multivitamin preparation per injection; 100,000 IU vitamin D/vial	3 vials/d per 20 d/3 mo: total exposure estimate = 18,000,000 IU 3 vials/d per 20 d/1.5 mo total exposure estimate = 9,000,000 IU

Serum Calcium	Serum 25(OH)D	Symptoms/Health Effects
3.5–3.7 mmol/L (~14 mg/dL)	496 ng/ml	Polydipsia, polyuria, anorexia, nausea; tx with IV saline, furosemide; hydrocortisone
3.75 mmol/L (15 mg/dL)	1,171 nmol/L (469.2 ng/ml)	Fatigue, constipation, back pain, forgetfulness, nausea, vomiting; tx with IV saline, furosemide, and pamidronate
3.95 mmol/L (15.8 mg/dL) (mean for adults at 5 weeks post-exposure)	58–60 IU/ml (145–150 ng/ ml) (5 weeks post-exposure)	Both adults developed renal failure. The female aborted a 10-week fetus at 3 weeks post-diagnosis for hypervitaminosis D. Plasma vitamin D levels were 60 IU/ml 5 weeks post-diagnosis; nephrocalcinosis persisted in the adult male but neither had long-term renal impairment
15.3 mg/dL	>150 ng/ml	Renal colic, confusion, lethargy, and weakness; reported passing small stones; tx with IV saline, furosemide, glucocorticoids
11.3 mg/dL	>150 ng/ml	

