INTRODUCTION:
Fluorine toxicity was first identified in the 1930’s and has subsequently been described from time to time in the literature.

Fluorine is present in phosphate rock or its derivatives that may be used in mineral supplements for farm animals and can be a by-product of industrial processes which may contaminate animal feeds and water supplies.

Diagnosis presents a challenge due to the natural levels of fluoride that occur in all animal tissue, with highest levels present in teeth and bones, and consequently the difficulty in interpreting laboratory results.

This article attempts to provide the veterinary practitioner with reference levels and also describes a case of suspected fluoride toxicity following the suspected exposure of a group of calves to gypsum intended for soil preparation for cropping.

FLUORIDE FORMS AND OCCURRENCE:
Toxic quantities of fluorides occur naturally in certain rock phosphates and the superphosphates, partially defluorinated phosphates and phosphatic limestones produced from them.

Forage crops grown on high-fluorine soils have increased levels due to mechanical contamination with soil particles.

Wastes from industrial processes, fertilizers, and mineral supplements are the most common causes of chronic fluorosis. The fluoride-containing gases and dusts from manufacturing of fertilizers, mineral supplements, metal ores (steel and aluminium), and certain enamelling processes may contaminate forage crops. Contamination of the surrounding area, particularly in the direction of the prevailing wind, may extend 8 – 9 km.

Sodium fluoride may be used to fluoridate water, and water from deep wells (boreholes) in certain areas may already contain high levels of fluorides.

Sodium fluoride has been used in anthelmintics for pigs and may still be encountered in cleaning agents e.g. laundry scour, certain specific metallurgy processes and it is used in “positron emission tomography”.

Volcanic ash has been reported to be high in fluoride

FLUOROSIS:
Botha CJ et al (1993) stated that high fluoride concentrations in ground water is a fairly common occurrence in South Africa, especially in large areas of the Springbok Flats, Gordonia, Namaqualand and the Kenhardt and Beaufort West districts.

Fluorosis in cattle due to the ingestion of a commercial lick was reported by Schultheiss and Godley (1995) and in the previous year Schultheiss and van Niekerk (1994) reported suspected fluorosis in a sheep flock in the Adelaide (Eastern Cape) area which was associated with a lick containing high fluoride levels.

Choubisa (1999) reported osteo-dental fluorosis in India associated with drinking water levels of 1.5 to 4 ppm and he found the prevalence of dental fluorosis was highest in calves less than 1 year of age which is consistent with Shupe (1980) who states that calves are more sensitive and less tolerant to fluoride. Age was reported to be associated with the greater prevalence of skeletal fluorosis.

Patra et al (2000) concluded that the consumption of fodder and water contaminated by the fumes and dusts emitting from superphosphate fertiliser plants resulted in the development of chronic fluorotic lesions in cattle and buffalo with dental discoloration, lameness, debility and some mortality.

Bourke and Ottaway (1998) investigated cattle mortalities in New South Wales in the vicinity of open-cut copper and gold mining. This was a retrospective study and they implicated fluorine in a drought lick
that contained gypsum as well as possible exposure to a gypsum store as part of a multifactorial problem that was not related to the mining enterprise.

According to Bourke and Ottawa (1998) impurities in phosphate gypsum include calcium fluorosilicate and trace amounts of miscellaneous elements.

These impurities may potentially render gypsum poisonous but the main ingredient, calcium sulphate may also be toxic. They report that while poisoning following the ingestion of calcium sulphate is poorly documented, it is possible that it could precipitate acidosis, hypercalcaemia, polioencephalomalacia, or secondary copper or selenium deficiency in ruminants.

Exposure to fluorides delays and alters mineralisation by replacing hydroxapatite in the crystalline structure of bone and mostly affects the matrices supporting formation of enamel, dentine, cementum and bone. Teeth are affected during development due to damage to ameloblasts and odontoblasts which fail to accept minerals normally.

Skeletal fluorosis interferes with formation of adequate matrix and mineralization by osteoblasts resulting in a dysfunction of normal sequences of osteogenesis, acceleration of bone remodeling, production of abnormal bone (exostosis, sclerosis) and in some cases, accelerated resorption. Abnormal and excessive bone formation leads to subperiosteal hyperostosis with thickened and irregular surfaces of long bones.

Several factors may interact to change the toxicity of fluoride in individual animal herds.
- Daily dosage or dietary concentration of fluoride.
- Total exposure time
- Availability of fluoride in the source ingested
- Age and species of animal exposed
- Nutritional factors

Fluoride toxicity is enhanced by poor nutrition and alleviated somewhat by high dietary intakes of calcium and aluminium.

Lesions occur first on the medial surface of the proximal third of the metatarsal and later on the mandible, metacarpals and ribs. The pelvis, vertebrae and other bones of the distal limbs are also affected. In chronically affected cattle, fracture of the digital bones in the medial claw is common, leading to lameness and a preference for affected animal to stand cross-legged. Articular surfaces and, depending on the level of exposure to fluoride and its concentration in bone, the bones may appear grossly and radiographically normal.

At highly toxic levels, the gross lesions of osteofluorosis occur rapidly and the new matrices produced are abnormal and remain unmineralized as in osteomalacia. Not only is any new bone abnormal, but it is apparently altered in its mechanical properties and it has a reduced life span.

It has been reported that in young, growing dogs and pigs fluorine intoxication produces lesions which, in many respects, resembles rickets and this may presumably occur in other species.

**SYMPTOMS:**
Fluorine toxicity may be presented in acute or chronic conditions.

Acute poisoning from inhalation of fluorine-containing gases or from ingestion of feeds or chemicals containing high levels of fluoride is rarely reported.

However, acute fluorosis may occur in ruminants if large quantities of fluoride are ingested over a short period. The clinical signs include salivation, inappetence, ruminal stasis, constipation or diarrhoea, dullness, dyspnoea and nervous signs. The fixation of serum calcium causes nervous symptoms characterised by an initial period of hyperaesthesia, muscle tremors, teeth grinding and ataxia. This is followed by sternal recumbency, depressed consciousness, dilated pupils, increased heart rate and eventually coma with bloating. Bourke and Ottawa (1998) suggest that if fluorine is ingested in a calcium-rich carrier such as gypsum (18 to 20% calcium) the nervous signs of hypocalcaemia may be absent and only inappetence, ruminal stasis, dullness and lethargy may be observed.

The signs of fluorosis from chronic ingestion are similar, regardless of the source of fluoride. At low toxic levels of intake the enamel of developing teeth may become chalky or mottled with staining and rapid and irregular wear. When exposure occurs after dental development has been completed, the teeth remain normal even if severe skeletal fluorosis develops. Clinical signs, apart from mild tooth lesions, occur in many animals when bone fluoride reaches 4,000 ppm and results in accelerated bone resorption and remodelling with production of exostoses and sclerosis. Metabolically active bones (ribs, mandible, and long bones) and growing bones in the young are most affected and the bones may become chalky white, soft, thickened, and as the condition advances developing exostoses may be palpated, especially along the long bones and on the mandible. Affected animals become lame and show a decrease in feed intake, water intake and weight gain. Severely diseased cattle may move around on their knees due to the pain from spurring and bridging of the joints in the late stages. When the skeleton becomes saturated (30-40 times normal bone content), “flooding” of
the soft tissue occurs, which results in a rise in plasma fluorides and metabolic breakdown of tissue associated with a loss of appetite and listlessness. J W Suttie (1983) suggests that at sufficiently high intakes, deciduous bovine teeth could be influenced but his investigations indicate that the "staining" or "brown discoloration" that is frequently reported was unrelated to fluoride ingestion, and these lesions should not be considered as definitive of bovine fluorosis.

During the winter of 2011 an eight month old calf that had been "walking on its knees" was presented to the authors for post mortem. The fetlock joints in this animal were severely affected with a degenerative arthritis. The calf was from a group grazing on maize stover (residues) and supplemented with a balanced formulated ration but may have had exposure to a pile of gypsum that had been placed in the area for use in soil preparation for the next crop. Subsequently, other calves from this group were reported to have exhibited lameness described as "laminitis like" but no hoof damage or poor hoof growth was evident and the calves responded to NSAID treatment with no subsequent detectable problems.

The calf that was post mortemmed had irregular stained and worn milk teeth (Figure 1.) and severe degenerative osteoarthritis (Figure 2.) of the fetlock joints. Joint lesions were characterised by small to larger multifocal erosions and ulcerations of the joint cartilage to large locally extensive areas of severe degeneration and necrosis of the cartilage. The subchondral bone was necrotic resulting in severe collapse of the normal joint architecture. Metatarsal bones had a level of 3528 mg fluoride per kg bone.

**DIAGNOSIS:**

In acute cases the clinical signs may be similar to milk fever and a thorough anamnesis may reveal exposure to a potential source of fluoride. Chronic cases may present as chronic debilitating arthritis and osteoporosis suggestive of deficiency or imbalances of calcium and phosphorus. Staining of teeth and lamenesses may be present but are not necessarily specific.

The diagnosis of a developing fluoride toxicosis may be assisted by the following tests and associated symptoms:

**1. Chemical analyses** to determine the amount of fluoride in the diet, plasma, urine, bones, and teeth. In cases of known ingestion, serum calcium and magnesium levels are beneficial. Urine fluoride levels are time dependent due to rapid elimination.

**2. Tooth effects**, in animals exposed at time of permanent teeth development;

**3. Lameness**, as the result of fluoride accumulation in bone; and

**4. Systemic evidence** as reflected by anorexia and cachexia. The adverse effects of fluoride exposure on growth and other nutritional parameters were more severe in calves fed low protein diets according to Jayant Lohakare et al (2010).

The following paragraphs describe various levels in animal tissues and feedstuffs as an aid to a diagnostic decision:

**1. Clinical pathology parameters**:

According to Merck Veterinary Manual the normal levels of fluorine in livestock are considered to be:

- <0.2 ppm in plasma,
- 1-8 ppm in urine,
- 200-600 in bones, and
- 200-500 in teeth.

Normal bovine urine contains <5 ppm fluorine; in borderline toxicity, urine contains 20-30 ppm, and in cattle with systemic signs, >35 ppm.

In cattle, toxicosis is associated with levels of >5,500 ppm in compact bone and >7,000 ppm in cancellous bone; in sheep, levels are believed to be lower (2,000-3,000 ppm in compact bone and 4,000-6,000 ppm in cancellous bone).

Shupe (1980) has suggested that the threshold for chronic fluorosis in cattle is a bone concentration of 1605 to 2794 mg/kg, depending on the age of the animal.

In the cases reported by Patra et al (2000) mean fluoride concentrations in serum and urine were

- 1.53 ±1.27 and 26.4 ±6.17 mg/L in calves below 1 year of age,
- 0.56±0.17 and 26.2 ±3.86 mg/L in cattle of 1 to 3 years,
- 0.49±1.13 and 27.5±4.63 mg/L in cattle above 3 years

These values were significantly higher than those of control animals and fluoride concentrations in the environmental sample collected from the affected locality were 534.4±74.9 mg/kg in fodder, and from 1.19 ±0.29 mg/L in pond water and 0.479 ±0.351 mg/L in well water.

**2. Feed and environmental parameters**

In South Africa feed levels are controlled by legislature as follows:

The Government Gazette dated 12 February 2010 dealing with undesirable substances in animal feeds controlled under the Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act, (Act no. 36 of 1947) states that the maximum content in mg/kg relative to farm feeds with a moisture content of 120mg/kg should not exceed 150 mg/kg with various exceptions. For example feed ingredients of animal origin should not exceed 500 mg/kg with the exception of marine krill which should not exceed 3000mg/kg.

Mineral supplements are controlled as follows:
Feed-grade phosphates must contain no more than 1 part of fluorine to 100 parts phosphorus. National Research Council suggests maximum tolerable fluoride concentrations 40 to 100 mg/kg (Nutrient Requirements of Beef Cattle seventh revised edition 1996 NRC National academy press page 55).

**TREATMENT AND CONTROL:**
Acutely exposed animals require calcium gluconate (IV) and oral magnesium hydroxide or milk to bind fluoride before absorption. In chronic exposure, control is difficult unless animals are removed from affected areas. It has been suggested that affected areas may be used for animals with a relatively short production life, e.g., pigs, poultry, or finishing cattle and sheep. Feeding calcium carbonate, aluminium oxide, aluminium sulphate, magnesium metasilicate, or boron has either decreased absorption or increased excretion of fluoride, and thus could offer some control of chronic fluorosis under some conditions. However, no treatment has been shown to cure the chronic effects of fluorine toxicity.

**DISCUSSION:**
In the case described above, the calf was in the high risk age group for fluorosis and exposure to gypsum was established. Since normal fluoride levels in bone are considered to be between 200 and 600 mg/kg, the threshold for a diagnosis of chronic fluorosis is 2794 mg/kg but with severe toxicosis being associated with levels > 5500 mg/kg it was hypothesised that the calves had taken in gypsum over a few days and that they had suffered from a form of subacute fluoride toxicity complicated by other undefined factors. Prozesky (2009) listed dietary factors that have been investigated as possible aetiological factors in osteochondrosis including imbalance in calcium-phosphorus levels, copper deficiency and metabolic acidosis amongst others. According to Bourke and Ottawa (1998) the exposure to calcium sulphate in the gypsum could precipitate hypercalcaemia, copper deficiency and acidosis aside from the potentially high fluoride levels. The exposure of the calves to the gypsum was accidental and they were prevented from gaining access to the gypsum after a few days. The gypsum that had been present, was not available for analysis having been dispersed in the lands before the calf showed clinical symptoms. Only the one calf showed severe clinical symptoms in terms of almost total loss of joint stability resulting in the inability to walk while the mildly affected calves recovered uneventfully.

The possibility exists of an interaction between high fluoride, calcium sulphate in the gypsum and a ration which itself may have been responsible for subclinical acidosis disrupting bone metabolism resulting in the described clinical symptoms. The symptoms and bone lesions were not necessarily typical of fluorosis alone. In spite of the circumstantial, clinical and pathological evidence in this case the authors felt that a definitive diagnosis of fluorosis could not be made but it raised many questions.

**CONCLUSION:**
Undesirable substances, such as fluoride, create a diagnostic challenge to the veterinary clinician. Commonly used feed additives such as lime and ammonium sulphate may hypothetically combine with borehole water, contaminated forage or inappropriate chemicals resulting in unpredictable clinical manifestations of mineral excess, deficit or even toxicities. While the case described was unable to be definitively diagnosed it is, however, hoped that this article will draw attention to these difficult diagnoses, supply some reference levels for the veterinary clinician’s convenience and prompt further investigations into the many possible problems that may be associated with undesirable substances in animal feeds.

**REFERENCES:**

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<td>Phosphates</td>
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<td>Calcium carbonate</td>
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<tr>
<td>Magnesium oxide</td>
<td>600</td>
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<tr>
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</tr>
<tr>
<td>Complementary feedstuffs containing more than 4% phosphorus</td>
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Figure 1: Deciduous teeth of an eight month old calf showing excessive and irregular wear and staining

Figure 2: Mild to severe multifocal to extensive lesions of articular cartilage degeneration, necrosis and ulceration

CPD QUESTIONS

1. Toxic quantities of fluoride occur naturally in the following:
   a. Phosphatic limestones
   b. Plants grown on high phosphate soils
   c. Effluent water from sewerage farms
   d. Meat and bone meal
   e. Pig anthelmintics

2. Fluoride toxicity in South Africa has been reported in association with:
   a. Ground water in the Eastern Cape
   b. Supplementary feeds of livestock
   c. Nitrate fertiliser application to forages
   d. Calves on high planes of nutrition
   e. All of the above

3. Toxic levels of Fluoride that are ingested and absorbed may cause:
   a. Accelerated resorption of bone.
   b. Dysfunction in the normal sequences of osteogenesis
   c. Accelerated bone remodelling
   d. Excessive subperiosteal hyperostosis
   e. All of the above

4. Symptoms of chronic Fluorosis are
   a. Less common than acute toxicity
   b. Always associated with feed supplements
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