AN UPDATE ON IRON AND SELENIUM IN ANIMAL NUTRITION

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IRON

Except for the elements sodium and chlorine in the form of common salt, iron has one of the oldest histories as an essential mineral element. Water containing an unusually high level of iron naturally (chalybeate water) was given as a treatment for anemia in people as early as the 1600's. Well before 1900, it had been demonstrated that iron was a component of hemoglobin. Compounds containing iron are currently used routinely as supplements of the element for both humans and domestic animals.

Iron Deficiency

Iron deficiency is a problem primarily with humans rather than with domestic animals. An exception to this is the baby pig which generally requires supplemental iron to maintain normal hemoglobin levels. Injectable preparations of iron dextran are given routinely to maintain normal body iron supplies in the piglet. Based on early research, it was suggested that grazing ruminants may become iron deficient. More recent observations indicated that if this does occur, it is more than likely due to loss of blood because of infestation with certain internal or external parasites. Such blood loss has a net effect of increasing the dietary iron requirement of these animals. Young ruminants depending mainly on milk or milk products in their diet may need supplemental iron to meet their requirement.

Research on dietary iron requirements for domestic animals is limited but, for animals under normal conditions, concentrations ranging from 30 ppm to as much as 100 ppm have been indicated (Table 1). For species where a range is given, the higher concentrations of dietary iron are indicated for the younger, growing animals within the particular species.

The iron content of a few representative feeds is shown in Table 2. Average iron concentrations in the grains shown varied from 30 ppm on a dry matter basis for corn grain to 85 ppm for barley and oat grain. The average iron content for dried citrus pulp was 99 ppm and standard sugarcane molasses contained 250 ppm on a dry basis. Typical protein supplements contained iron ranging from about 130 ppm for soybean meal to 225 ppm for cottonseed meal. Milk products are an exception to this and the average value for dried skim milk was 10 ppm.

Forages also contain relatively high concentrations of iron, although information is rather limited. In results summarized in Table 2 (NRC, 1982), iron in alfalfa varied from an average of about 250 ppm iron on a dry matter basis when it was in the early vegetative stage of growth to about 150 ppm when it was in full bloom. An average value given for Coastal bermudagrass was 300 ppm iron. Ammerman et al. (1982) reported that Suwanee bermudagrass varied in iron

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content from more than 80 ppm at two weeks regrowth to about 35 ppm at twelve weeks regrowth.

A comparison of dietary iron requirements with iron present in various feedstuffs (Tables 1 and 2) seems to substantiate the general observation that iron deficiency is not a serious problem in most domestic animal species especially after the animal has begun to supplement its milk diet with typical grains and forages. Information does seem to be limited, however, with regard to influence of plant species, plant maturity, soil etc. on the iron content of forages.

Iron Toxicosis

More recently there has been greater interest in the potential detrimental effect of excessive intakes of dietary iron. Physiologically normal animals can restrict iron absorption and are usually well protected against relatively high dietary intakes of the element. Dietary maximum tolerable iron concentrations have been indicated to range from 500 ppm for sheep and horses to as much as 3000 ppm for swine (Table 1; NRC, 1980). In that publication, maximum tolerable level, is defined as "that dietary level that, when fed for a limited period, will not impair animal performance and should not produce unsafe residues in human food derived from the animal." Coupled with that definition are the following statements. "It is in keeping with good nutritional practice to maintain the mineral intake at required levels, which generally are well below the maximum tolerable levels. Continuous long-term feeding of minerals at the maximum levels may cause adverse effects."

Pitzen (1993) proposed that excessive levels of dietary iron may contribute to total oxidative stress experienced by the animal resulting in reproductive and health problems. This statement is based on field observations made in several dairy herds in which production records were kept and feed and water were analyzed for several trace minerals. In herds where excessive iron intake was occurring, major contributors to dietary iron intake included the supplemental iron source, the supplemental calcium phosphate source and in some cases the water supply. Based on experiences in the field with dairy herds, this author suggested that "Prooxidant related health and breeding problems are common when the iron concentration in forages fed exceeds 400 ppm." Apparently no liver iron values were obtained to give an indication of the actual iron overload which may have occurred in the cows.

One theory of the aging process in humans is that it is due to oxidation of cell membranes and that too much "free iron" in the body's cells can lead to this oxidation and destruction. Under normal physiological conditions in the body and with reasonable intakes of iron, the iron circulating within the system is essentially all bound to protein. Free, ionized iron under these conditions is at a minimum. In addition, under normal conditions, iron within the cells is either protein bound or is present in chemical structures which prevent it from being a cause of oxidation. Thus, the animal body, under normal conditions, is buffered against the adverse effects of iron over a range of intake of the element well above its requirement. If this level of iron intake is exceeded, or if the body fails to handle iron in the normal way, then elevated levels of iron have the potential for causing oxidative destruction within the tissues.

Rosa et al. (1986) observed a depression in feed intake and body weight gain in growing lambs when 1000 ppm supplemental iron as ferric citrate was fed. Further depression occurred when 40 ppm supplemental copper as cupric chloride was added to this diet. When 1000 ppm supplemental zinc as zinc basic carbonate was combined with the other two elements, much of the reduction in both feed intake and body weight gain was overcome. This may have resulted from bringing the dietary iron and zinc into better balance. Based on lower levels of iron in livers of lambs fed the diet, it appeared that the elevated zinc resulted in less iron being absorbed. In studies with mice fed extremely high dietary iron (3000 to 8000 ppm), increased vitamin E was useful as an antidote for iron toxicosis (Omara and Blakely, 1993). The results suggested that depletion of body stores of vitamin E due to excessive iron may be a factor in toxicity of the element.

Iron in Water

Water can provide significant quantities of iron to the diet of domestic animals (NRC, 1974). The concentration of iron in natural waters varied greatly with a mean value of 43.9 µg/L and a range of 0.1 to 4,600 µg/L for 1,836 samples of surface water collected in the United States between 1957 and 1969 at 140 locations. At maximal concentrations of iron with average intakes of water, it was estimated that the water could contribute 12 to 60% of the dietary iron required by domestic animals. It is anticipated that iron carried in solution would be of high bioavailability while that present in particulate matter would be less well utilized as influenced by its chemical form. Concentrations of iron in subsurface waters were not listed in the NRC publication.

Iron in Phosphates

Feed grade phosphates contain significant quantities of iron and this iron can be considered in the formulation of diets. Ammerman et al. (1993) indicated that, for one set of phosphate samples, the average iron content varied from 0.79% for tricalcium phosphate (defluorinated phosphate) to 0.89% for a monocalcium/dicalcium phosphate product (Table 3). The range in iron content for individual feed grade phosphate samples was from about 0.4 to about 1.2%. Thus, if as much as 1% of the phosphate were added to a diet, total iron in the diet provided by the phosphate would vary from 40 to 120 ppm. Based on research with swine and poultry, it appears that bioavailability of iron present in phosphates may vary from about 55% for tricalcium or defluorinated phosphate to perhaps 70% for monocalcium/dicalcium phosphate (Table 4). If one assumes an average iron bioavailability of 50% for all feed grade phosphates for all domestic animal species, the phosphate source can supply a significant portion of the total dietary iron requirement.

Summary

Iron, as an essential mineral element, is of much greater concern with regard to the possibility of a deficiency with humans than it is with domestic animals. A deficiency of dietary iron is of great concern, however, in the young nursing pig and may be of concern in the young of other species when their diet is based primarily on milk or milk products. Dietary iron toxicosis can occur in domestic animals particularly when the drinking water contains high levels of soluble iron. Iron levels in many feeds are such that adequate dietary levels will be provided to the animal without the need for supplemental sources. The bioavailable portion of the iron present in feed grade phosphates should be considered in diet formulation.

SELENIUM

The early interest in selenium with regard to domestic animals related almost entirely to its toxicity. The toxicity of selenium became well established and this history appears to have had a profound influence on the general acceptance and use of selenium even after it was established as a dietary essential mineral element.

Essentiality

Selenium has been recognized as essential since Schwarz and Foltz demonstrated in 1957 that it was effective in preventing liver degeneration in rats. Very soon thereafter, selenium was shown to prevent exudative diathesis in chicks (Patterson et al., 1957; Schwarz et al., 1957) and nutritional muscular dystrophy in calves (Muth et al., 1958) and lambs (Hogue, 1958).

Dietary Requirements and Deficiencies

Dietary requirements by domestic animals for selenium are shown in Table 1. These concentrations vary from about 0.05 to 0.30 ppm depending on species and class of animal within species. They were developed by the National Research Council (NRC) Subcommittees on Nutrient Requirements for the various species. The NRC Subcommittee on Selenium in Nutrition also concluded that the minimal dietary selenium requirement probably falls within the 0.05 to 0.30 ppm range (NRC, 1983).

Numerous researchers have shown that forages and grains grown in the United States are frequently deficient in selenium and this is verified by signs of the deficiency becoming evident in animals. In a major survey of plant material grown in the United States, Kubota and Allaway (1972) reported deficient levels of selenium in forages and grains in vast areas of the eastern and western portions of the country. Although not completely true, it can be indicated that, in general, the sections of the United States west of the Rocky Mountains and east of the Mississippi River will yield plant material containing deficient to adequate levels of selenium while that part of the country between the Rocky Mountains and the Mississippi River will produce plant material containing adequate to toxic levels of selenium.

Food and Drug Administration Regulations

Once selenium was established as an essential element and its deficiency in domestic animals under practical feeding conditions was recognized, an effort was begun to obtain approval from the Food and Drug Administration (FDA) for its use as a dietary supplement. Approval for supplemental use of selenium came slowly and in a piecemeal manner to say the least. This was due, in part, to the well known toxicity of selenium and to the unfounded belief that it might be carcinogenic. Initial approval by FDA for the use of selenium came in 1974 some 17 years after it had been shown to be essential. This approval allowed for supplemental concentrations of selenium from either sodium selenite or sodium selenate not to exceed 0.1 ppm for swine and growing chicken diets and up to 0.2 ppm for turkeys. The selenium approval process has been described in detail by Ullrey (1980; 1992) and all appropriate references are found in his papers.

Even though selenium had been shown to protect against white muscle disease in young ruminants in 1958, the approval obtained in 1974 did not provide for the use of supplemental selenium for ruminants. In 1979, approval was extended to 0.1 ppm supplemental selenium to beef cattle, dairy cattle and sheep. Approval was granted by FDA for selenium supplements of 0.1 ppm to diets of laying hens in 1981 and, in 1982, approval was given for supplemental levels up to 0.3 ppm in prestarter and starter diets for swine. Then, in 1987, FDA granted an increase in supplemental selenium from 0.1 to 0.3 ppm in complete feeds for all major food producing animals. In 1989, the regulations were amended to allow the use of a sustained release selenium supplement in the form of a bolus containing sodium selenite to be placed in the reticulorumen of beef and dairy cattle.

Following approval of the higher supplemental levels of selenium in 1987, objections began to be raised on the basis of a potential negative environmental impact due to the allowed elevated levels of the element. Objections were filed in 1989 by several organizations stating that potentially adverse environmental effects had not been evaluated adequately at the time the regulation was published in 1987. Response by FDA included a hearing in Washington on August 25, 1992 involving the environmental impact of selenium in animal feeds. About one year later, September 13, 1993, the Agency published that it was staying the regulation of 1987 and thus, in effect, returning the approved use levels of selenium in animal feeds to those that were permitted before 1987 (FDA, 1993). The effective date for this change was the date of issuing the regulation. The FDA also stayed the 1989 regulation which provided for the use of a bolus for selenium supplementation but indicated that regulatory action against the sale or use of this product would not begin for a period of eight months after the September 13, 1993 date.

The level of supplemental selenium currently allowed is based on the amendment to the regulation published January 26, 1979 (FDA, 1979). For beef cattle and dairy cattle, it states the following:

Beef cattle:
(i) In complete feed at a level not to exceed 0.1 part per million.
(ii) In a feed supplement for limit feeding at a level not to exceed an intake of 1 milligram per head per day.
(iii) Up to 20 parts per million in a salt-mineral mixture for free choice feeding at a rate not to exceed an intake of 1 milligram per head per day.

Dairy cattle:
In complete feed (total ration) at a level not to exceed 0.1 part per million.

The level of selenium is so low in feeds grown in many parts of the United States that present FDA regulations do not allow for sufficient supplemental selenium to be provided to meet the animal's nutritional requirement for the element. This suggests a situation somewhat similar to that years ago when it was necessary to distribute feeds based on known origin in an effort to meet the animal's requirement for selenium. Appropriate use of approved injectable forms of selenium under the supervision of a veterinarian may be helpful in providing more nearly adequate amounts of the element. This situation with selenium is apparently the first time a FDA regulation has been in direct conflict with meeting the nutritional needs of domestic animals.

Summary

The early interest in selenium related primarily to its toxicity. Its reputation as a toxic element plus the concern that it might be carcinogenic delayed FDA approval of the supplemental use of selenium in domestic animals. This delay occurred even after selenium was observed to be a dietary essential element and after serious deficiencies of the element were demonstrated under many practical feeding situations. The first approval by FDA for supplemental dietary use of selenium in swine and poultry came in 1974. Following various amendments which allowed its supplemental use in beef cattle, dairy cattle and sheep, FDA in 1987, granted an increase in the supplemental level of selenium from 0.1 to 0.3 ppm in complete feeds for all major food producing animals. In September, 1993, the 1987 amendment to the regulation was stayed meaning that the currently approved supplemented level of selenium is 0.1 ppm for swine, sheep, cattle and most classes of poultry. This regulatory inhibition makes it very difficult to meet the dietary nutritional requirement for selenium in many situations.

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Table 1. Dietary requirements (Req.) and maximum tolerable levels (MTL) of iron and selenium for domestic animals (ppm)

Element	Item	Beef Cattle	Dairy Cattle	Sheep	Swine	Poultry	Horse
Iron	Req.[1]	50-100	50-100	30-50	80	50-80	40-50
	MTL[2]	1000	1000	500	3000	1000	(500)
Selenium	Req.[1]	0.05-0.30	0.30	0.1-0.2	0.15	0.1-0.2	0.1
	MTL[2]	(2)	(2)	(2)	2	2	(2)

[1]References for beef cattle, dairy cattle, sheep, swine, poultry and horse are NRC (1984a), NRC (1989a), NRC (1985), NRC (1988), NRC (1984b) and NRC (1989b), respectively. Values listed for beef cattle, dairy cattle and horses indicated as "suggested values", "recommended contents" and "adequate concentrations", respectively.

[2]NRC (1980). Listed toxic concentrations (MTL) were derived from data on the designated species, while those in parentheses were derived from interspecific extrapolation.

Table 2. Iron content of representative feeds[1]

Feed	Iron, ppm (Dry matter basis)
Energy feed	
Barley grain	85
Citrus pulp	99
Corn grain	30
Oat grain	85
Sorghum grain	51
Sugarcane molasses (79.5 degree brix)	250
Wheat grain	58
Protein supplement	
Cottonseed meal (solv. extd.)	223
Dried skim milk	10
Peanut meal (solv. extd.)	154
Soybean meal (solv. extd.)	133
Forage	
Alfalfa (early vegetative)	253
Alfalfa (early bloom)	192
Alfalfa (full bloom)	150
Coastal bermudagrass	300

[1]NRC (1982) except for dried citrus pulp. Values for citrus pulp from Ammerman et al. (1968).

Table 3. Usual guaranteed phosphorus content and analyzed iron concentration of feed-grade phosphates[1]

Phosphate	Phosphorus, %	Iron, %[2]: Mean ± SD[3]	Iron, %[2]: Range
Monocalcium/dicalcium	21.0	0.89 ± 0.26	0.4 - 1.2
Dicalcium/monocalcium	18.5	0.84 ± 0.21	0.4 - 1.1
Tricalcium	18.0	0.79 ± 0.15	0.5 - 1.0
Monoammonium	24.0	0.84 ± 0.29	0.4 - 1.2

[1]Ammerman et al. (1993).
[2]Values represent more than 100 samples for each phosphate and represent products from the major U.S. feed phosphate manufacturers. Data provided by Pitman-Moore, Inc., Mundelein, IL.
[3]Mean ± standard deviation.

Table 4. Relative bioavailability of iron from phosphates[1]

Iron source	Swine[2]		Chickens[3]	Chickens[4]	
	Hb[5]	Hc[5]	Hb	Hb	Hc
Ferrous sulfate regent grade	100	100	100	100	100
Monocal/dical phosphate	-	-	61	66	76
Dical/monocal phosphate	-	-	55	-	-
Tricalcium phosphate	54	58	44	48	51

[1]Ammerman et al. (1993).
[2]Kornegay (1972). Value based on relative comparison of final values after subtraction of response with basal diet
[3]Deming and Czarnecki-Maulden (1989). Value based on slope ratio.
[4]Henry et al. (1992). Value based on slope ratio.
[5]Hb=Hemoglobin; Hc = Hematocrit.