Vanadium Mining and Cattle Health

Sentinel studies, epidemiological and veterinary public health issues

(met een samenvatting in het Nederlands)

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Chapter 1

GENERAL INTRODUCTION

B. Gummow

The White Rabbit put on his spectacles. "Where shall I begin, please your majesty?" he asked.
"Begin at the beginning," the King said gravely, "and go on till you come to the end; then stop." - Carroll (1865)
**Vanadium: What is it?**
The chief credit for the discovery of vanadium must be given to Nils Gabriel Sefström, who when working on a sample of iron ore from Taberg in Sweden, recognised an unusual constituent, whose salts could be prepared from slags resulting from the treatment of cast iron. In 1831 he succeeded in making an oxide of an entirely new element. Because this formed beautiful multicoloured compounds, his assistant Berzelius named it vanadium, after Vanadis the legendary goddess of beauty from the far north. The separation of the element from its salts proved a hard task and it was only in 1869 that Roscoe was able to tell the Royal Society of the isolation of a little powdery vanadium, of 95.8% purity (Faulker Hudson, 1964). However it was not until 1927, nearly 100 years after its discovery, that Marden and Rich (1927) made the first ductile metal of 99.7% purity.

Vanadium is classified as a transition element on the periodic table with the atomic number 23. It has a molecular weight of 50.94, a melting point of 1890 °C and boils at 3380 °C. It has six oxidation states (l-, 0, 2+, 3+, 4+, and 5+) of which 3+, 4+, and 5+ are the most common (CRC handbook of chemistry and physics, 1977).

**Where is vanadium found?**
Vanadium is widely distributed in nature and the average level of vanadium in the earth’s crust is normally 100-150 ppm (Faulker Hudson, 1964; Richie, 1985; Waters 1977). The prevalence of vanadium exceeds that of such well-known metals as copper and lead (Nriagu, 1998), and equals that of zinc and tin (Byerrium et al., 1974; Windholz, 1983; Greyson, 1983). Vanadium compounds exist in over 50 different mineral ores at concentrations of between 10-4100 ppm and in association with fossil fuels, particularly coal (at concentrations of between 19-126 ppm in ash) and crude oil (at concentrations of between 3-257 ppm) (Nriagu, 1998). There are few ores from which vanadium can be recovered economically as a single product.

Most of the vanadium production comes as by-products and co-products in the extraction of other elements such as iron, phosphorus, and uranium. Ores from which vanadium can potentially be recovered are found in many parts of the world. About one third of the vanadium resources are located in Africa and North America, and about 24% are found in Europe and <4% in both Asia and South America (Nriagu, 1998). About 83% of vanadium recently
produced from mines comes from vanadiferous magnetite ($\text{Fe}_3\text{O}_4$) in South Africa, China and Russia (Hilliard, 1992). The remaining 17% of worldwide vanadium production from primary sources is recovered from the oil industry.

South Africa is the world's leading producer of vanadium and accounts for 50% of the current global output. Other producing countries include Russia, China and the USA. Western Australia has large deposits of magnetite ores containing vanadium, and the tar sands of Alberta, Canada, represent a huge reservoir of vanadium (Nriagu, 1998). These sources of vanadium remain largely untapped.

**Industrial use and economic importance of vanadium**

The vanadium oxides are most often used by industry, primarily in the manufacturing of steel, where it is used as ferrovanadium or as a steel additive (Reilly, 1991; Toxicological profile for Vanadium, 1992). It has good corrosion resistance to alkalis, sulphuric and hydrochloric acid, and salt waters, but the metal oxidizes readily above 660 °C. Vanadium is thus used in producing rust-resistant, spring, and high-speed tool steels. It is also used in the production of components for aircraft engines and weapon systems, making it a strategic mineral for armament manufacturers. In addition, because the metal has good structural strength and a low-fission neutron cross-section, it is useful in nuclear applications.

Vanadium foil is used as a bonding agent in cladding titanium steel. Vanadium pentoxide is used in ceramics and as a catalyst. It is also used as a mordant in dyeing and printing fabrics and in the manufacture of aniline black (CRC handbook of chemistry and physics, 1977). Small amounts of vanadium are used in making rubber, plastics, and certain other chemicals (Reilly, 1991; Toxicological profile for Vanadium, 1992).

**The presence of vanadium in living organisms**

When examining various fruits, vegetables and plants, Bertrand (1941) detected vanadium in all the 62 specimens studied. He found its average concentration in the higher plants to be 1 ppm, roots usually containing more than seeds and leaves; root nodules of most leguminous plants had about 4 ppm, occasionally up to 12 ppm. Fungi contained less, usually 0.5 ppm, but exceptionally as much as 112 ppm.
Vanadium is found in high concentrations in certain marine organisms, particularly ascadians and sea-squirts belonging to the family tunicates. It seems that many of these creatures accumulate the element in their blood, gut and other tissues. It is thought that vanadium may function as a form of oxygen carrier in these animals in the same way that erythrocrurorin of invertebrates, chlorocruorin, the green blood pigment of certain annelid worms; haemerythrin in spinuculds worms; and haemocyanin in various molluscs and arthropods act as oxygen carriers. Unlike haemoglobin and haemovanadin, these pigments are not confined to blood cells but are present in the plasma as conjugated proteins, having a metal incorporated in the molecule (Faulkner Hudson, 1964; Nriagu, 1998).

Vanadium is also found in a wide variety of tissues of higher vertebrate animals. Puls (1989), gives a summary of vanadium levels found in cattle, sheep, dogs, pigs, chickens and ducks. Normal liver concentrations for cattle are reported as 6-7 \( \mu \text{g/kg} \) (wet weight). These appear to be much lower than the liver concentrations reported for sheep (100—220 \( \mu \text{g/kg} \)), dogs (30-50 \( \mu \text{g/kg} \)) and chickens (18-38 \( \mu \text{g/kg} \)) but of the same order as ducks (0.7-2 \( \mu \text{g/kg} \)).

Various people have looked for vanadium in human tissues (Koch \textit{et al.}, 1956; Perry & Perry, 1959). One of the more rigorous studies using emission spectrography was done by Tipton (1960). Her specimens were taken at autopsy from the victims of sudden death, usually from trauma and sometimes from cardiovascular and other diseases. The tissues examined were aorta, brain, heart, kidney, liver, lung, ovary, pancreas, prostate, spleen, and testis, all of which appeared macroscopically normal. In a very small percentage of specimens, vanadium could be found in the liver, prostate and spleen. In about half the specimens it was found in the lungs. The average concentration in these organs was usually less than 1 mg of vanadium/kg of ashed material, except for the lung, which had levels of up to 5 mg/kg.

**Vanadium as an essential trace element and therapeutic agent**

Vanadium has been shown to be an essential trace element for a variety of animal species (Puls, 1989). Vanadium deficiency is associated with stunted growth, impaired reproduction, altered red blood cell formation and iron metabolism and changes in blood lipid levels. There is a growing belief among health experts that the metal can play a similar role in humans.
During the 1980’s, vanadium was reported to mimic the metabolic effects of insulin in rat adipocytes (Lu et. al., 2001). In the 1990’s, vanadium was found to act in an insulin-like manner in muscle and liver as well. Subsequent studies revealed that the action of vanadium salts is mediated through insulin-receptor independent alternative pathways. The investigation of the antidiabetic potency of vanadium soon ensued. Vanadium therapy was shown to normalise blood glucose levels in STZ-rats and to cure many hyperglycemia-related disorders. Therapeutic effects of vanadium were then demonstrated in type II diabetic rodents, which do not respond to exogenously administered insulin (Goldwaser et. al., 2000). Overcoming vanadium’s toxicity, has however, remained the major obstacle in using vanadium as a therapeutic agent.

Several reviews describe the interactions of vanadium with tissues, cells and enzymes in more detail (Rehder, 1992; Dafnis & Sabatini, 1994; Leonard & Gerber, 1994; Zelikoff & Cohen, 1995; Nriagu, 1998).

**Vanadium as a pollutant and its toxic effects**

*Biochemical effects*

It has long been known that vanadium is toxic to both man and animals and many of the symptoms of acute poisoning were already described at the turn of the 20th century. Yet the pathogenesis of vanadium poisoning is still poorly understood. Scientists are only now beginning to understand the biochemistry of vanadium and with this understanding, the pathogenesis of vanadium poisoning is gradually being unravelled. It has been established that certain forms of vanadium are more toxic than others (Table 1) and we now know that vanadium is capable of modifying the activity of a number of enzymes, including Na and K-ATPase, which is important in muscle contraction, tyrosine kinase, which is located in growth factors, oncogenes, phosphatases and receptors for insulin (Berner et. al. 1989, Nriagu, 1998). Vanadium also inhibits the enzyme cholinesterase, which results in deficiency of choline and affects the metabolism of the sulphur-containing amino acid cysteine. The vanadate and vanadyl ions (Table 1) further inhibit Ca and Mg-ATPase, which are important in synaptosomal membranes in nervous tissue as well in facilitating muscle contraction (Nriagu, 1998).
Table 1 Toxicologically significant vanadium compounds

<table>
<thead>
<tr>
<th>Name of compound</th>
<th>Chemical Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanadium pentoxide</td>
<td>V₂O₅</td>
</tr>
<tr>
<td>Sodium metavanadate</td>
<td>NaVO₃</td>
</tr>
<tr>
<td>Sodium orthovanadate</td>
<td>Na₃VO₄</td>
</tr>
<tr>
<td>Vanadyl sulphate</td>
<td>VO₃S₄</td>
</tr>
<tr>
<td>Ammonium metavanadate</td>
<td>NH₄VO₃</td>
</tr>
</tbody>
</table>

Toxicity in man

Dietary vanadium does not appear toxic to man, at least at low levels normally encountered in foods. Industrial exposure of workers to vanadium dusts is a well-recognised occupational hazard. Vanadium pentoxide (V₂O₅) dust is usually encountered in occupational settings, and the primary route of exposure for humans is via inhalation. Responses to industrial exposure are thought to be acute rather than chronic, involving irritation of the eyes and respiratory system in the form of conjunctivitis, bronchospasm, bronchitis and asthma-like symptoms. An estimated 25 % of soluble compounds may be absorbed from the lungs (WHO, 1987; Lauwerys & Hoet, 1993). V₂O₅ is specifically reported to be nearly 100 % absorbed by inhalation (Lewis, 1995). Information on the effects of the other vanadium compounds comes mainly from oral studies in animals. Absorption via the oral route appears to be low (Friberg, 1979).

Other symptoms of vanadium poisoning described in humans include weakness, nausea, vomiting, anorexia, tinnitus, headache, dizziness, green discolourisation of the tongue, palpitations, transient coronary insufficiency, bradycardia with extra systoles, dermatitis, anaemia, leucopenia, leukocyte granulation and lowering of cholesterol levels (Faulkner Hudson, 1964; Hunter, 1975; Friberg, 1979; Reilly, 1991). Recent studies in humans have shown that correlations existed between the vanadium levels in urine and serum and cognitive deficits. When vanadium concentrations were around 14.2 µg/l in urine a reduction in
neurobehavioral abilities were observed, particularly visuospatial abilities and attention (Barth et al., 2002).

The long-term effects of exposure in humans do not appear to have been extensively studied (Toxicological Profile for Vanadium, 1992; SIMRAC, 2000).

Biomarkers specific for exposure to vanadium include the presence of vanadium in the urine (Gylseth et al. 1979; Kiviluoto et al. 1981; Lewis, 1959; Orris et al. 1983; Zenz et al. 1962) and a green discoloration of the tongue (Lewis, 1959), the latter resulting from the direct accumulation of vanadium pentoxide.

**Toxicity in monogastric animals**

A considerable amount of work has been done on vanadium over the years using monogastric animals as models. These began as long ago as 1876 when Priestley (1876) showed that sodium vanadate solutions, when given by various routes, was intensely poisonous to the pigeon, guinea-pig, rabbit, cat and dog (Faulkner Hudson, 1964). He found that 9.18-14.66 mg V$_2$O$_5$/kg could kill a rabbit when injected subcutaneously. It was apparent in these experiments that vanadium had two chief modes of action; a central effect on the nervous system causing drowsiness with convulsions, followed by a gradual paralysis of respiration and motion, and an effect on the alimentary tract causing abdominal pain, with diarrhoea and bloody stools. These original observations have been confirmed by others (Puls, 1989). Proescher, Seil & Stillians (1917), went on to use both large and small experimental animals, including birds and fish, and some of these results are reported by Faulkner Hudson (1964). The LD$_{50}$ in rats, injected subcutaneously with ammonium metavanadate, has since been estimated more precisely at 22.7 mg V$_2$O$_5$/kg (Massmann, 1956). The horse and rabbit were shown to be especially sensitive to vanadium, while the rat and mouse were relatively resistant. Jackson (1911 and 1912) showed that vanadium, when administered intravenously to dogs, produces intense vasoconstriction in the spleen, kidney and intestine, with associated rise in temperature. The dominant findings of this early work were therefore the depression of the respiratory centre, marked vasoconstriction of the visceral arteries, and inflammatory lesions in the lung, kidney and intestine. A summary, which includes more recent work, is given by Puls (1989) and differs little from the original work carried out. All these observations however, were based on acute or subacute exposure,
usually by iatrogenic means. Until recently little work had been done to examine the effects of low dose, long term exposures. One of the first long term studies to be carried out in rats and mice was published as recently as 2001 (National Toxicology Program technical report, 2001) and because of the nature of the results, there has been some debate over the methodology used. The study reported neoplastic effects for the first time in the form of bronchiolar and alveolar adenoma or carcinoma in rats that had been exposed to inhalation of 2 mg/m$^3$ $V_2O_5$ for 2 years. No genetic toxicity however, could be shown when using Salmonella typhimurium gene mutations. The other lesions described in this study were non-neoplastic lesions of the nose, larynx, and lung in the form of epithelial hyperplasia, inflammation, fibrosis and alveolar histiocytosis. There don’t appear to have been any studies of this duration carried out in other animal species or man.

Toxicity in ruminants

The work in this thesis looks in more detail at the effects of exposure to vanadium in ruminants. Prior to this study little work had been done in ruminants and those studies that had been carried out appear to have been primarily acute or sub-acute experimental studies or field outbreaks, usually involving exposure to high doses of vanadium. Hansard et al. (1978, 1982a, 1982b, 1982c) did a number of studies using sheep. They found that in sheep doses of 9.6-12 mg vanadium / kg body weight given in a gelatine capsule an hour after feeding caused a decline in feed intake and diarrhoea. Necropsy of these animals showed extensive mucosal haemorrhage of the small intestine and diffuse subcapsular haemorrhages of the kidneys. No difference in toxicity could be shown between ammonium metavanadate, calcium orthovanadate and calcium pyrovanadate. A dose of 40 mg NH$_4$VO$_3$ / kg body weight in gelatine capsules caused death in two out of three sheep within 80 hours.

One of the first experimental studies on vanadium poisoning in cattle was that of Platonow and Abbey (1968). These were acute experimental studies carried out in calves and are the ones usually referred to by others when vanadium toxicity in cattle is described (see Chapter 2 for a more detailed description of signs in cattle). Frank et al. (1996) reports an earlier paper published in 1964 of toxicity in cows that ingested fuel oil soot (ter Heege et. al., 1964). Frank et al. (1990) reported acute vanadium poisoning of cattle in northern Sweden after grazing on pastures fertilized with basic slag and followed this work up in 1996 with a second paper on the
event that included tissue levels in cattle slaughtered in other parts of Sweden as well (Frank, et al. 1996). McCrindle, et al. (2001) reported on acute vanadium poisoning in cattle illegally grazing in an area where a vanadium spill had occurred on a South African mine.

**Comparative kinetics of vanadium**

Animal data (Conklin et. al., 1982; Oberg et. al. 1978; Rhoads & Sanders, 1985; Roshchin et. al. 1980) and limited human data (Diamond et. al. 1963; Gylseth et. al. 1979; Schroeder et. al. 1963) are available on the kinetics of vanadium. From studies done in humans, rats, mice, and dogs it would appear that vanadium kinetics between monogastric animals and humans are similar. Despite this however, as with any particulate substance, extrapolations on inhalation absorption rates from animals to humans is still difficult. Only one set of kinetic studies appear to have been done in ruminants (sheep). From these studies it appears that the kinetics in ruminants may be slightly different to those of monogastric animals due to the difference in the physiology and anatomy of the rumen versus stomach (Patterson et al., 1986). Significant absorption of vanadium occurs from the upper gastro-intestinal-tract (GIT) of sheep and concentrations of vanadium in the upper and lower GIT of sheep were respectively ten and hundred fold greater than in the blood (Patterson et al., 1986).

**The relationship between vanadium mining and cattle farming in South Africa**

Although vanadium poisoning is uncommon, vanadium forms a large component of the mining industry in South Africa and increasing concern is being expressed about the impact of this industry on livestock in South Africa (Wates, 1996). South Africa is one of the world’s greatest sources of vanadium and has a substantial amount of industry associated with vanadium mining and processing. The areas where these mining and processing industries are located are in many cases the same areas that farmers utilise for farming. However, there appears to have been little work done in ruminants with respect to vanadium exposure. Yet, all the documented field outbreaks of vanadium toxicity in livestock in South Africa have involved cattle and the mining industry (Unpublished archival records of the Onderstepoort Veterinary Institute, Private Bag X05, Onderstepoort, 0110, 1961/1962, 1975/1976, McCrindle, 2001).
Very little is known about the effects of chronic low dose exposure of cattle to vanadium or what constitutes safe grazing for cattle in areas of the country where vanadium is known to occur.

The use of cattle as environmental sentinels for the mining industry
The primary goal of an animal sentinel system is to identify harmful chemicals or chemical mixtures in the environment before they might otherwise be detected through human epidemiological studies or toxicological studies in laboratory animals. Once identified, exposures to them could be minimised until methods can be devised to determine specific aetiological agents or until suitable prophylactic measures can be established. Animal sentinel systems might provide additional valuable time in which to search for the answer.

Animal sentinel systems therefore have potential value as early warning systems for new hazards, as indicators of potential human exposure to complex mixtures or in complex environments, and as monitors of the effectiveness of remedial measures or other environmental management actions. In these applications, data from animal sentinels are usually used qualitatively, but there is at least potential for semi-quantitative assessments.

Animal sentinel data should include data obtained from epidemiological (descriptive and analytic) studies and from animal and food chain monitoring programmes. Data from animal sentinel studies can often be obtained more quickly than data from human epidemiological studies, because the ideal sentinel responds to toxic insults more rapidly than humans do (long before clinical manifestations of disease) and at environmentally relevant doses. In addition, animal sentinels, like humans, are simultaneously exposed to complex and variable mixtures of chemicals and other environmental agents. Some environmental mixtures have been shown to be more toxic than would be predicted based on their principal chemical constituents (Hornshaw et al., 1983). These characteristics of animal sentinel studies offer important advantages over laboratory animal studies, in which animals are usually exposed to high, constant doses of a single chemical substance that is under investigation. Thus, the use of animal sentinels constitutes an approach to identifying hazards and estimating risks in circumstances similar to those in which actual human or surrounding animal exposures occur.
For example, animal sentinels were used as a community and public health tool in a study of sheep living around a zinc smelter in Peru. This study demonstrated the feasibility of establishing animal sentinels around point sources of pollution (Reif et al., 1989). Heavy-metal exposures were documented in sheep pastures up to 27 Km downwind from the smelter. A mortality database for the population of 177 000 sheep was used in an attempt to relate heavy-metal burdens to health effects, including cancer. No relationship between hepatic arsenic concentrations and other heavy metals was found for pulmonary adenocarcinoma, a neoplasm hypothesised as a priori to be related to arsenic exposure.

Other industries where cattle have been successfully used as sentinels are those that produce fluoride. These industries include aluminium, steel and copper smelting, chemical manufacture, ceramic production, and coal-based electricity generation (Shupe et al., 1979). Dairy and beef cattle near such facilities have been severely affected by fluorosis because of airborne contamination of forages. These animals have acted as suitable sentinels of fluoride emissions and have been used by industry and regulatory agencies to assess the effectiveness of emission control measures.

More recently, reindeer in the Arctic and other foraging animals were used as sentinels of radioactivity resulting from the April 1986 nuclear-reactor accident at Chernobyl, USSR, by virtue of the radioactivity in their flesh and milk (National Research Council, USA, 1991).

In South Africa, cattle proved to be a suitable sentinel for detecting copper air pollution originating from a copper smelting plant, long before pollution monitoring authorities using conventional methods were aware that pollution was indeed taking place (Gummow et al., 1991).

Despite these examples, most uses of domestic animals to monitor environmental pollutants have been unplanned by-products of veterinary services directed at alleviating health problems in the animals involved, rather than organised monitoring programmes. Few programmes for using healthy domestic animals as biologic monitors have until recently been proposed (Swabe et al., 1971; Buck, 1979). The work in this manuscript serves as an example of an organised monitoring programme.
Scope of the thesis

In 1990, a farmer began experiencing losses amongst his calves, which were literally wasting away before dying. The private veterinarians consulted were at a loss as to what the cause of the problem could be. Initially they thought it might be copper deficiency due to high background molybdenum levels. The farmer was also blamed for poor husbandry and eventually an epidemiologist (the author) was called in to try and solve the problem. A disease outbreak investigation was carried out to find out what the cause of this “new disease” could be and the results of this investigation are published in Chapter 2. This was the first published article on vanadium poisoning in South Africa and the work went some way to try and resolve the pathogenesis of vanadium poisoning in cattle, which is still poorly understood.

Faced with a vanadium-contaminated environment, an attempt was made to find a prophylactic treatment for the farmer. No treatments for vanadium poisoning had ever been tried in ruminants before and so an experimental study was designed to test one of the treatments reported to have been successful in mice, calcium disodium ethylenediamine tetraacetate. The results of this attempt at finding a suitable prophylactic treatment for cattle are published in Chapter 3. In doing this work it became apparent that a lot more knowledge of the disease in cattle was needed before a suitable prophylactic treatment was likely to be found.

In 1998, a vanadium spill at another mining site resulted in the death of some communal cattle. It was uncertain if the deaths were due to vanadium but the mine compensated the farmers for their losses, despite the fact that the cattle were trespassing on mine property. This resulted in a flurry of claims against the mine by surrounding farmers. Having heard of the previous work done during the 1990 outbreak, the mine approached the author (B. Gummow) for a solution that would indicate whether the mine was putting the surrounding farmers’ cattle at risk or not. From this was born the idea of running a sentinel herd of cattle on the mine’s property, with the objectives of studying the chronic effects of vanadium, of seeing whether cattle were in fact being affected by mining operations, and whether cattle could be used as an early warning system for detecting problems in pollution control. This had never been done before and the concept of farming was as foreign to the mining industry as the concept of mining was to the veterinary profession. To sell this idea to the mine was unique on its own; to set up a trial that
would meet these objectives required many hurdles to be overcome, beginning with the infra-
structure and management of the cattle on a mine.

It soon became apparent that methodology did not exist that would enable a reasonably accurate
measure of how much vanadium the cattle were taking in. Existing plume dispersion models
took no account of oral intake, which was a major component of intake for cattle. Failure to get
an accurate assessment of intake would mean that no assessments of risk could be made. The
methodology for this took two years to develop as it involved inputs from experts in the mining
field, physicists, chemists, soil scientists and veterinarians. Finally a working model that
encompassed environmental and physiological inputs was created and a novel way of
quantifying intake of vanadium was developed. This model is applicable not only to vanadium
studies but can also be used for other environmental pollution studies involving similar
hazardous substances. Details of the model are presented and discussed in Chapter 4. The model
allowed for the first time an estimation of the no-adverse-effect-level for vanadium in cattle.

Acceptance of the model by independent referees allowed the exploration of other questions
that were arising as a result of the research. The mining industry had been using urine as a
biomarker of exposure for many years, yet it was always suspected that this was an unreliable
biomarker. Was this really the case? If cattle were to be used as sentinels, what should be
measured that would indicate problems? If cattle died from vanadium poisoning, could tissue
concentrations of vanadium be used to make a diagnosis? The question of biomarkers therefore
became of increasing importance for both veterinarians and the mining industry. For this reason,
a wide spectrum of tissues and blood parameters were monitored at great expense in the hope of
finding a better way of monitoring vanadium exposure in both animals and man. The results of
this work are discussed in Chapter 5.

If cattle were being exposed to higher vanadium levels around mining or industrial areas in the
world or even in areas just rich in vanadium, did this pose any threat to the consumer?
Particularly as adult cattle from these areas showed little evidence of vanadium poisoning and
the milk and meat of these cattle was entering the food chain even though calves were
becoming ill. Chapter 6 discusses public health aspects of farming cattle in areas rich in
vanadium.
Finally the question of cattle health and the pathogenesis and treatment of chronic vanadium poisoning in cattle needed to be looked at in greater detail. These were the consequences of being exposed to chronic intake of vanadium. Some aspects of this are mentioned in the general discussion (Chapter 7), but this work is ongoing and still to be written up and properly evaluated.

References


CRC Handbook of Chemistry and Physics, 1977. CRC Press, Cleveland, Ohio.


General introduction


Chapter 1


