VANADIUM AIR POLLUTION: A POSSIBLE CAUSE OF "ILL-THRIFT" IN DAIRY CATTLE

B. GUMMOW (Faculty of Veterinary Science, University of Pretoria, Private Bag X 04, Onderstepoort, 0110, South Africa), STELLA. S. BASTIANELLO, C.J. BOTHA & A. T. BASSON

Introduction

In April 1990 the Veterinary Research Institute (VRI) at Onderstepoort was approached by a private veterinarian to do an epidemiological study into the cause of "ill-thrift" occurring in a dairy herd in the eastern Transvaal, South Africa.

Materials and Methods

The investigation was undertaken at 3 time intervals - April 1990 (late Autumn), January (mid Summer) and June 1991 (mid Winter). During the 3 visits environmental factors, history, and clinical signs within the population were examined.

Environment: To test an initial hypothesis of copper (Cu) deficiency due to high background levels of molybdenum (Mo), soil and grass samples were taken at 10 and later 12 points on the farm. At each point ± 500 g of surface soil, deep soil (30 cm) and grass in the immediate vicinity of the soil samples were collected. The samples were collected at the intervals given above.

An alloy processing plant (Plant) was situated immediately adjacent to the farm and it was therefore decided to include within the analysis profile iron (Fe), chromium (cr) and vanadium (V) to rule out environmental pollution as a cause. The samples collected in April 1990 were thus analyzed for Fe, Cu, zinc (Zn), cr, Mo and V, using standard methods for atomic absorption spectrophotometry (Perkin-Elmer Corporation, Norwalk, Connecticut, USA). The samples collected in January and June 1991 were analyzed for only Cu, Fe and V.

Animals: Ten to 25 animals were clinically examined during each farm visit. On the second visit, animals were randomly selected from various age groups: 3 (0-3 m), 5 (4-7 m and 8-11 m), and 6 (heifers, dry cows and lactating cows). Animals selected on the third farm visit were the same animals that were selected on the second visit with additional animals included. The numbers and age groups were as follows: 9 (0-3 m), 5 (4-7 m and 16-19 m), 4 (12-15 m and a group comprising cattle that had previously aborted), and 11 (adult cows > 19 m). Intravenous blood was collected from these animals to determine the following parameters: Total serum protein (TSP), albumin (Alb), globulin (Glob), blood urea nitrogen (BUN), gamma-glutamyltransferase (GGT), aspartate aminotransferase (AST), creatine phosphokinase (CK), white cell count (WCC), red cell count (RCC), haematocrit (Ht), and blood glucose. Blood obtained on the third farm visit was also tested for blood creatinine (Cr) levels and lymphoblast transformation responses to plant lectins. Faeces was collected from 19 adult cattle during the second farm visit to determine faecal V levels.

Organ analysis for vanadium: Between May 1990 and September 1991, tissues from 7 calves (< 13 m old) and 2 adult cows, all of which had exhibited signs of ill-thrift, were analyzed for their V content using standard methods[1]. The data are summarised in Table 2.

Pathology: Necropsies were performed on 4 calves and 2 adult cattle that were showing signs of "ill-thrift" prior to necropsy. Formalin fixed tissues from a further 5 calves were examined histopathologically.

Results and Discussion

Soil analyses: The soil V results are shown in Table 1. The results of the first farm visit showed that Cu, cr, Mo and Zn were not present in excessive levels in the vegetation

or soil on the farm. All three investigations showed low Cu and high Fe levels. Their pattern of distribution showed no correlation to distance or direction from the Plant implying that these minerals occurred naturally on the farm and reflecting what should be seen if no air pollution was taking place.

TABLE 1: VANADIUM LEVELS (ppm DM) OF SOIL AND GRASS IN RELATION TO DISTANCE AND DIRECTION FROM PLANT

Camp No.	Distance km	Direction	Autumn			Summer			Winter			Mean V Levels		
			Surface	Deep	Grass	Surface	Deep	Grass	Surface	Deep	Grass	Surface	Deep	Grass
3	0.32	N	1055	206	290	745	461	27	991	115	180	930	261	166
2	0.49	NNW	514	508	31	313	127	4.9	204	152	85	344	262	40
4	0.52	N	274	198	8	1122	338	9.7	522	155	75	639	230	31
5	1.43	N	149	93	10	333	256	0	86	67	70	189	139	27
12	1.49	ENE	-	-	-	328	264	4.6	182	127	0	255	196	2
11	1.56	WNW	-	-	-	67	59	10.8	36	31	0	52	45	5
6	1.88	NNW	58	41	12	120	80	0.8	67	98	30	82	73	14
10	1.92	WNW	44	18	0	70	36	10.3	50	36	30	55	30	13
9	2.14	WNW	42	41	0	51	51	0.6	48	54	0	47	49	0
1	2.40	W	35	22	3	92	57	0.8	61	39	20	63	39	8
7	2.73	NNE	354	215	0	558	590	4.3	263	247	20	392	351	8
8	2.86	N	385	291	15	494	361	1	165	283	30	348	312	15

The average level of V in the earth's crust is normally 100-150 ppm [5,20,22]. Of the 12 camps sampled camps 3, 2, 4, 5, 12, 7 & 8 had above normal levels of V on average in the surface soil. All these camps were situated either adjacent to the Plant or north to north-east of the Plant, with the exception of camp 2 which was more north-west but which bordered on the Plant. None of the other camps to the west or north-west of the Plant had abnormally high levels of V suggesting a link between direction from the Plant and V levels. Since the predominant wind direction was towards the north-east our findings indicated that the Plant was a probable source of V pollution.

If the surface soil V levels are examined in terms of distance from the Plant then a definite trend could be shown which indicated that the further from the Plant the lower the V levels. This link between distance from the Plant and soil V levels also suggested that the Plant was a possible source of V pollution.

Camps 7 & 8 appear to have inconsistent results as they are far from the Plant, yet have high levels of V in the soil. These high levels could be ascribed to the topography of the farm in that although these camps were further from the Plant than camps 5 & 6 they were at the same altitude as camps 3 & 4 and the Plant making it possible for pollution from the Plant to overshoot camps 5 & 6, which were situated in a valley, and settle on camps 7 & 8.

In those camps north and north-east of the Plant the V levels in the deep soil were, on average, always lower than the surface soil levels. Such a finding is inconsistent with soil naturally rich in V, and lead to the assumption of V air pollution. The most likely source of this was the adjacent Plant. In those camps north-west of the Plant the difference between the deep and surface V levels was virtually negligible, which is what is expected if there was no aerial pollution.

Camps 4, 5, 7, 8 & 12 had much higher levels in the soil during summer than winter. This is the converse of what occurred in the grass samples and suggested that during the high rainfall summer months much V that may have been trapped on the grass was washed into the soil resulting in higher soil levels during summer and lower grass levels. This finding supported a postulation of air pollution. The seasonal variation could explain why there was no cumulative effect over the sampling period.

Grass analyses: Grass V levels showed a decrease with distance from the Plant (Table 1). The highest levels were closest to the Plant. This finding supported the postulation that the source of the V was the Plant. The grass iron levels showed no correlation with distance but a good correlation to soil levels and illustrated what would be expected if air pollution was not playing a role.

The low V grass levels in camps 7 & 8 suggests that there was little correlation between soil levels of V and aerial grass levels. Normal levels of V in higher plants are given as an average of 1 ppm [5,17,22]. The average levels on the farm all exceeded 1 ppm with the exception of camp 9. Most of the farm therefore had abnormally high levels of V in

or on the grass. The highest levels occurred in camp 3, closest to the Plant, with an average of 166 ppm. Seven of the 12 camps sampled had average levels greater than 10 ppm.

Higher levels of V occurred on the grass during winter than summer. This trend fits a postulation of aerial pollution as it can be assumed that during the rainy season dust particles will be washed off the grass resulting in lower levels on the grass.

Little work has been done to determine the toxic level of V for cattle in grass. Fox (1987) specifies that a typical feedlot diet for cattle contains ± 0.57 ppm V and estimates that the maximum tolerable dietary level of V for cattle is 50 ppm[4]. Most of the camps on this farm exceeded 0.57 ppm and those camps closest to the Plant far exceeded 50 ppm. It is therefore possible that grass levels alone on certain parts of the farm were high enough to cause toxicity in cattle. Unfortunately experimental feed trials that describe V toxicity were usually carried out over fairly short periods of time[5,12,17] and there is no data to establish the chronic effects of low doses of V.

The grass analyses showed that the north side of the Plant had high V grass levels which did not appear to be coming from the soil and therefore probably arose from the air. Aerial samples collected by the Centre of Scientific and Industrial Research supported this. Since animals are constantly outside they can potentially breathe in large quantities of V from the air and when grazing may breathe in V present in the dust near the ground. As inhalation is recognised as one of the major routes of V toxicity in humans, inhalation of V in cattle cannot be ignored when considering V intake. From the results it is known that some V was ingested with the feed. It could not be determined how much V was being inhaled.

Clinical signs: Signs of ill-thrift occurred primarily in 0-12 m calves and comprised: poor growth, emaciation, intermittent diarrhoea, sub-mandibular oedema, pot-belly, lacrimation/conjunctivitis, rhinitis, congested mucous membranes, intermittent fever, dull staring hair coats and stiff gait. Animals became progressively weaker over a varying time period before dying of cachexia. Force-feeding failed to reverse the course of the disease. Some animals have survived for more than a year despite being severely stunted. They tend to walk stiffly and are not as active as other animals of similar age.

All these signs are consistent with the signs described for V toxicity[4,5,6,7,8,12,17,21,22]. Similar signs can be associated with a variety of conditions and considerable effort was taken to exclude the following differential diagnoses: poor management practices, poor genetic material, poor ration quality and quantity, unbalanced rations, verminosis, paratuberculosis, chronic arsenic poisoning, gossypol poisoning, Vit E/Se deficiency, bovine viral diarrhoea, Brucella, Campylobacter, Leptospira infections and Cu, Zn, Mo toxicities and deficiencies. It is postulated that the underlying cause of the signs was a malabsorption problem coupled to an immunosuppression phenomenon.

At the onset of the investigation no clinical signs were noted in the adult cows. However over the last 6 months there was a dramatic rise in abortions, stillbirths and neonatal mortalities. Necropsies on 4 foetuses and 1 neonate failed to reveal any specific aetiology. Pregnant cows have never experimentally been exposed to V so there is no evidence to show whether V can cause stillbirths in cattle. Wide (1984) reports an increased frequency in spontaneous abortions in Finnish women that was correlated to exposure to Al, Co, Mo and V in metal industries[23]. She also found evidence that a single dose of V could interfere with foetal skeletal ossification in pregnant mice. Hence there is evidence that V can have an effect on the developing foetus, but the effects of chronic exposure to V are unknown. As no evidence could be found that any of the common causes of abortion were playing a role on the farm it was assumed, by a process of elimination, that V was possibly the cause of the stillbirths. The farmer also reported that at about the same time as abortions occurred there was a drop in milk production in his herd. These findings correlated with a previous report from the Bon Accord area of South Africa (1962) of V toxicity (unpublished VRI archival data).

Pathology findings: The gastrointestinal tract (GIT), lymphoid and haemopoeitic tissues, and respiratory system in both calves and adults were primarily affected.

The principal macroscopic finding was a moderate to severe cachexia with associated

atrophy of fat depots, skeletal muscles and parenchymatous organs. A mild to moderate anaemia was also present. The GIT lesions included: dry watery ruminal contents, spilling-over of grain into the abomasum, mucoid small intestinal contents, soft caecal or soft to hard, dry colonic and rectal contents, and, occasionally rectal dilatation. The findings suggested that a high proportion of the ingested V, known to be retained within the GIT (Table 2), interfered with motility and uptake of nutrients. Vanadium does interfere with active transport and uptake of Na^+ and K^+ and its presence in the GIT lumen could therefore interfere with active absorption of nutrients causing a malabsorption syndrome and eventual cachexia[2,12,13,19].

The histopathological findings of moderate to severe villous atrophy, characterised by fusion and blunting of villi, and a moderate granulomatous enteritis and typhlocolitis also lend support to the theory of a malabsorption syndrome. As these lesions were subacute to chronic in nature, they imply a chronic ingestion of V. Similar lesions have been reported in pigs[21].

In all 7 cattle necropsied there was moderate to severe atrophy of the spleen and superficial lymph nodes and in 2 cases atrophy of the bone marrow. These lesions may have been a reflection of the generalised atrophy and cachexia but histopathologically there were few or no germinal centres in the cortices of the lymph nodes and splenic white pulp and those present were hypocellular and inactive on appearance. The latter changes suggest hypo-activity of the lymphoid cells and correlate with the findings of decreased in vitro lymphocytic activity.

The respiratory lesions were minimal, focal in distribution and characterised histologically by alveolar collapse, alveolar or septal emphysema, and in 1 calf bronchiectasis and metaplasia of the terminal bronchioles. The above lesions are chronic in nature and suggest a prolonged exposure to V air pollution. In humans exposed to V dust, respiratory symptoms and lesions are commonly encountered[4,22].

Organ and faecal analysis for vanadium

The V levels in the faeces of the heifers, dry cows and milk cows during the second farm visit ranged from 2.1-8.8 ppm with a mean of 4.5 ppm ± 2 (n=19). There was no significant difference between groups. The organ levels obtained during the period of investigation are shown in Table 2.

Table 2: Results of organ analysis (ppm WM)

Animal no.	Age	Liver	Kidney	Bone	Rumen	Date
10	11 m	0.4	2.1	2.8	1.3	May 90
11	11 m	0.1	0	2.4	2	May 90
9	10 w	0.3	0	1.3	4	Oct. 90
15	< 12 m	0.7	0.2	-	1	Jan. 91
16	< 12 m	2	0	-	0	Jan. 91
8	2 w	0	0	-	4	June 91
17	< 12 m	-	-	-	2.6	Jan. 91
19	4 y	0	0	-	23	Sept. 91
18	7 y	0	0	-	27	Sept. 91

Limit of detection = 0.05 ppm; Not determined = -

Normal tissue V levels for cattle are reported to be in ppb (ng/g) and the level for liver is given as 0.006-0.007 ppm (WM)[18]. The levels of V in bone and liver were consistent with what has been described for V toxicity while those of the kidney were not[5,6,7,15,18]. There are no reference values for rumen content but the fact that V was consistently found in the rumen of the dead animals and faeces of living animals supports a postulation of V toxicity.

Clinical pathology findings: The main thrust of the clinical pathology was to try and establish underlying causes for the symptomatology and pathological findings that had been found. The areas concentrated on were: a) evidence that may indicate organ damage b) evidence to support a malabsorption syndrome and c) evidence to support an immunosuppressive effect.

I. **Evidence to Support Organ Damage:** The enzymes used to assess liver damage were GGT and AST, neither of which were abnormally high for any of the groups studied. There was

therefore little evidence of acute liver damage in the herd.

The enzyme used to test for muscle damage was CK. Raised levels of CK were seen in the 0-3 and 12-15 m old groups. This would support evidence of muscle breakdown as would occur in a cachexic state.

Indicators used to assess kidney function were BUN and Cr. A decrease in BUN was seen in individuals in all the age groups. The prevalence of low BUN levels increased with increasing age. All animals 12-19 m or which had aborted showed low BUN levels. This finding supports the postulation made by others that V causes an increased glomerular filtration rate[5,10,16]. The Cr levels increased with increasing age and all the animals in the 12-19 m group had abnormally high Cr levels. High Cr levels together with high BUN levels are usually an indication of glomerular damage. However non-Cr chromogens may cause false high values and the most significant of these are ketones[3]. Animals that are energy deficient such as would occur with malabsorption could therefore have false high Cr levels. Since the BUN levels were not raised the latter explanation for high Cr is more feasible than glomerular damage and would give added evidence for malabsorption.

II. Evidence for Malabsorption: The parameters used to assess malabsorption were blood glucose and TSP and its various fractions. The blood glucose levels were on the whole normal except for the adult group where over half the animals had decreased levels.

The TSP levels were low in all the 0-3 m calves and in the majority of animals in the 4-7, 8-11, 12-15 and 16-19 m groups. The adult cattle had normal TSP levels. The albumin:globulin (A/G) ratio in the 0-3 m group was on the whole normal indicating that the low TSP levels were as a result of low levels of both alb and glob. This would occur with protein losing enteropathies, malabsorption, malnutrition or chronic liver disease together with immunodeficiency and/or failure of passive colostral transfer. The 4-7 m and 8-11 m groups showed an increase in A/G ratio due to a decrease in glob levels, which would support an immunodeficiency. Hence the low TSP values in animals < 12 m appeared to confirm a diagnosis of malabsorption and immunodeficiency as supported by the pathology. It is interesting to note that it was only the calves that showed an overall decrease in TSP and it was only these animals that showed severe signs.

Thereafter the A/G ratio tended to decrease with increasing age. In the 12-15 m and 16-19 m groups this decrease was primarily due to a decrease in alb suggesting a protein-losing enteropathy in this group but not immunosuppression as the glob fraction was normal. The adult animals had low A/G ratios but these appeared to be due to an increase in glob levels rather than a decrease in alb levels suggesting an over-stimulation of the immune system in adult cattle.

Glob fractions were also examined for each age group. The 0-3 m group showed a deficiency in gamma globulin (τ-glob) levels which supported the findings of malabsorption and immunodeficiency. The 4-7 m and adult cattle groups showed a low τ-glob fraction and a high ß-glob fraction. The ß-glob fraction represents transferrin, ß-lipoprotein, complement-3 and some immunoglobulins[3]. It is reported that V competes with iron for transferrin[14,15,16,19] and it can therefore be assumed that with V toxicity there would be an extra demand for transferrin causing more of it to be produced and thus higher serum levels. The high ß-globs could therefore be as a result of increased transferrin which would be consistent with a diagnosis of V toxicity. Similar findings were seen in the 12-15 m and 16-19 m groups with the additional finding of a low α-glob fraction which together with the low τ-glob fraction strengthens the argument for immunosuppression.

III. Evidence for Immunosuppression: Cellular immunity was examined by means of differential WCC. The WCC were above normal in all the age groups studied implying that some form of chronic immune stimulation was taking place. The only groups where all the animals did not have high WCC were the 0-3 m and 4-7 m groups.

From 4-12 m there is evidence of a lymphocytosis which becomes less common in the adult cattle. High lymphocyte counts are usually a reflection of white cell production and function and are associated with chronic infections. Hence there appears to be evidence of a chronic stimulation of the immune system in the majority of the animals in the herd. Persistent exposure to V dust could theoretically act as such a stimulant.

An increase in immature neutrophils was seen in the 0-3 and 4-7 m groups and the 4-7 m group also showed an increase in mature neutrophils.

A monocytosis was seen in all the age groups <15 m and >19 m but was most obvious in the 4-7 m group. Causes of monocytosis include, protozoal infections, suppuration, haemolysis and immune injury[3]. A monocytosis therefore fits in with evidence to support some form of immune injury.

The absence of eosinophils in all groups gave added evidence that helminths were not playing a significant role on the farm.

A puzzling question was why were there so many white cells if the animals were immune compromised? To try and solve this problem in vitro tests were carried out to establish how active the lymphocytes were[11]. Twenty cattle were examined, 10 calves < 7 m and 10 cows > 19 m. None of the adult cows had normal lymphoblast transformation responses to plant lectins and only 4 of the calves showed a response but which was nevertheless suppressed. Hence although the lymphocytes were present they were not active implying that V was possibly preventing them from responding normally.

A further finding supporting V toxicity was the presence of Heinz bodies in the erythrocytes of cattle less than 7 m but not in adult cattle. Heinz bodies usually indicate an impairment of the glucose-6-phosphate dehydrogenase pathway or a depletion of glutathione[3]. Glutathione is thought to reduce vanadate to vanadyl and thus render it less toxic[5,9,10]. Continual exposure to V could thus lead to a deficiency in glutathione and result in denaturation of haemoglobin leading to Heinz bodies.

Although the clinical pathology results cannot be used alone to make a diagnosis, it becomes clear from them that they support evidence for malabsorption and immunosuppression as well as V toxicity.

Conclusions

Due to the vague nature of the clinical signs of V toxicity and the lack of definitive diagnostic tools for this disease it is very difficult to conclusively prove that an animal has died or is suffering from V toxicity. What this investigation did was accumulate a library of circumstantial evidence which lead us to believe that the animals on the affected farm were suffering from the effects of excessive levels of V. Where it was thought that another known disease may result in a similar picture steps were taken to satisfy ourselves that such a disease was not playing a role. In this way we feel confident that V toxicity was the underlying cause of the ill-thrift problem experienced on the farm.

Because little has been published on the effects of V air pollution on animals there are few precedents upon which to base our results. We have accumulated circumstantial evidence suggesting that air pollution was taking place on the farm and that the source of the air pollution was the adjacent Plant.

On the basis of all our findings we conclude that there was sufficient circumstantial evidence to make a diagnosis of V toxicity which was most probably caused by air pollution from the nearby Plant.

References

1. BOYAZOGLU, P.A., BARRETT, E.L., YOUNG, E. & EBEDES, H., 1972. Liver mineral analysis as an indicator of nutritional adequacy. Proceedings of the 2nd world congress of animal feeding, Madrid, Spain, 795-1008. 2. BRACKEN, W.M. & SHARMA, R.P., 1985. Cytotoxicity-related alterations of selected cellular functions after in vitro vanadate exposure. Biochemical Pharmacology, 34, 2465-2470. 3. DUNCAN, J.R. & PRASSE, K.W., 1986. Veterinary Laboratory Medicine. Iowa State University Press, Ames, Iowa, USA. 4. FOX, M.R.S., 1987. Assessment of cadmium, lead and vanadium status of large animals related to the human food chain. Review. Journal of Animal Science, 65 (6), 1744-1752. 5. FAULKNER HUDSON, T.G., 1964. Vanadium: toxicology and biological significance. Elsevier Publishing Company, London. 6. HANSARD, S.L., AMMERMAN, C.B., FICK, K.R., & MILLER, S.M., 1978. Performance and vanadium content of tissues in sheep as influenced by dietary vanadium. Journal of Animal Science, 46, 1091- 1095. 7. HANSARD, S.L., AMMERMAN, C.B., HENRY, P.R. & SIMPSON, C.F., 1982. Vanadium metabolism in sheep. 1. Comparative and acute toxicity of vanadium compounds in sheep. Journal of Animal Science, 55, 344-349. 8. HANSARD, S.L., AMMERMAN, C.B. & HENRY, P.R., 1982. Vanadium metabolism in sheep. II. Effect of dietary vanadium on performance, vanadium excretion and bone deposition in sheep. Journal of Animal Science, 55, 350-356. 9. HANSEN, T.V., AASETH, J. & ALEXANDER, J., 1982. The effect of chelating agents on vanadium distribution in the rat body and on uptake by human erythrocytes. Archives of Toxicology, 50, 195-202. 10. HEINZ, A., RUBINSON, K.A. & GRANTHAM, J.J., 1982. The transport and accumulation of oxyvanadium compounds in human erythrocytes in vitro. Journal of Laboratory Clinical Medicine, 100, 593-612. 11. KRISTENSEN, F., KRISTENSEN, B. & LAZARY, S., 1982. The lymphocyte stimulation test in veterinary epidemiology. Veterinary Immunology & Immunopathology, 3, 203-277. 12. KUBENA, L.F. & PHILLIPS, T.D., 1986. Toxicology of vanadium.

Federation Proceedings, 45, 128. **13.**MACARA, I.G., KUSTIN, K. & CANTLY, L.C., 1980. Glutathione reduces cytoplasmic vanadate. Mechanism and physiological implications. Biochimica et Biophysica Acta, 629, 95-106. **14.**NECHAY, B.R., 1984. Mechanisms of action of vanadium. Annual Reviews Pharmacology and Toxicology, 24, 501-524. **15.**NECHAY, B.R., NANNINGA, L.B., NECHAY, P.S.E., et al, 1986. Role of vanadium in biology. Federation Proceedings, 42 (2), 123-124. **16.**PATTERSON, B.W., HANSARD, S.L., AMMERMAN, C.B., HENRY, P.R., ZECH, L.A. & FISHER, W.R., 1986. Kinetic model of whole-body vanadium metabolism: studies in sheep. American Journal of Physiology, 251, R325-R332. **17.**PLATONOW, N. & ABBEY, H.K., 1968. Toxicity of vanadium to calves. The Veterinary Record, 292-293. **18.**PULS, R., 1988. Mineral levels in animal health: Diagnostic data. Sherpa International, Clearbrook, BC, Canada. **19.**RAMASARMA, T., MACKELLAR, W.C. & CRANE, F.L., 1981. Vanadate-stimulated NADH oxidation in plasma membrane. Biochimica et Biophysica Acta, 646, 88-98. **20.**RICHIE, D.A., 1985. The effects of toxicity induced by feeding selected elements (Pb, Hg, Cd, F, V). Agri-Practice, 6 (1), 37-42. **21.**VLEET, J.F. van., BOON, G.D. & FERANNS, V.J., 1981. Induction of lesions of selenium-vitamin E deficiency in weanling swine fed silver, cobalt, tellurium, zinc, cadmium and vanadium. American Journal of Veterinary Research, 42, 789-799. **22.**WATERS, M.D., 1977. Toxicology of vanadium. Advanced Modern Toxicology, 2, 147-189. **23.**WIDE, M., 1984. Effect of short-term exposure to five industrial metals on the embryonic and fetal development of the mouse. Environmental Research, 33, 47-53.

Acknowledgements: ATTENDENCE OF THIS CONFERENCE WAS MADE POSSIBLY BY **SMITHKLINE BEECHAM ANIMAL HEALTH & PFIZER SOUTH AFRICA.**