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REVIEW ARTICLES AND NOTES

SELENIUM-RESPONSIVE DISEASES OF ANIMALS IN NEW ZEALAND

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INTRODUCTION

UNTIL recently, interest in the biology of selenium was focused on its properties as a naturally-occurring poison in plants grazed by stock in certain problem areas, notably in the western states of North America. The geological distribution of soils bearing seleniferous vegetation, the toxicities of various forms of selenium, including those of its inorganic salts, and the treatment and prevention of selenium poisoning have been dealt with in detail by Rosenfeld and Beath (1964), and those aspects will not be considered further in this review.

Since 1957, an entirely new role for selenium, as a factor in the prevention of certain nutritional diseases of animals, has emerged. Evidence indicating that selenium can now be regarded as an essential trace element for animals has been reviewed by Underwood (1962). However, because of the possibility that factors additional to a deficiency of selenium may be of importance in the aetiology of enzootic diseases controllable by selenium, in this review the term "selenium-responsive" will be used to designate those conditions.

To explore the potential significance of selenium in world livestock production, United States workers (Wolf *et al.*, 1963) conducted a survey among principal agricultural research centres at home and abroad. Results indicated that selenium-responsive diseases were of world-wide distribution. In addition, a number of other workers have reviewed selenium-responsive conditions in livestock with particular reference to investigations carried out in their own countries. Among the overseas investigators concerned, mention may be made of the Oregon group in the U.S.A. (*e.g.*, Schubert *et al.*, 1961), and of workers in the United Kingdom (*e.g.*, Blaxter, 1962) and in Western Australia (Gardiner *et al.*, 1962).

Selenium-responsive diseases in New Zealand were reviewed previously, some six years ago (Hartley and Grant, 1961; Cousins and Cairney, 1961). The purpose of the present review is to give an up-to-date account of selenium as it affects animal health in New Zealand and to present this against a background of what is known concerning the physiological function and metabolism of the element.

PHYSIOLOGICAL FUNCTION AND METABOLISM OF SELENIUM

Historically, interest in selenium as an essential trace element stems from overseas studies on vitamin E (α-tocopherol) deficiency diseases. Following the discovery of that vitamin 45 years ago, it was established that, according to the nature of the diet and kind of experimental animal used, the consequences of a deficiency of vitamin E included infertility, failure to grow optimally, exudative diathesis, necrosis of the liver, kidney or heart, myopathy, or combinations of these. Subsequently, it was found that a second factor, L-cystine, also gave some protection against certain vitamin E deficiency states.

About 10 years ago, overseas workers (Schwarz and Foltz, 1957) announced the important discovery that, in addition to vitamin E and cystine, very small amounts of selenium would protect against experimental dietary liver necrosis in the rat. In the same year, Patterson *et al.* (1957) reported that selenium effectively controlled growth depression, mortality, and exudative diathesis in chicks. Following on this, a

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number of agricultural workers in different countries established that certain enzootic myopathies in cattle and sheep could be controlled by the administration of selenium, and that, in this respect, selenium appeared, usually, to be more effective than was α-tocopherol.

The history of selenium-vitamin E relationships has been reviewed by Moore (1962), and Schwarz (1961) has summarized the development of investigations into the potent selenium-containing factor which he has termed "Factor 3". Factor 3 has been found to be present in kidney, liver, brewer's yeast and numerous other natural source materials. The position of cystine is at present unclear. It appears that its biopotency is, at least in part, attributable to the fact that samples normally contain selenium as a trace contaminant, although Schwarz and his group consider that selenium-free sulphur amino acids, in general, have a delaying effect on onset of disease. The precise chemical nature of Factor 3 has not been reported. It appears that, at least in kidney, there are two different components with Factor 3 activity (designated α- and β- Factor 3) and that, possibly, α-Factor 3 is an aliphatic seleninic or selenonic acid. As compared with known selenium compounds given in equivalent amounts, Factor 3 has a greater biopotency for the prevention of liver necrosis in rats.

Elucidation of the mode of action of selenium is an exceedingly complex problem. Not only may quite different manifestations of selenium responsiveness occur in the same species, but there exist groups of diseases, experimental or enzootic, some of which appear to respond only to selenium, others only to vitamin E, and yet others to either selenium or vitamin E (see Schwarz, 1961). It has long been known that vitamin E has antioxidant properties. Furthermore, a remarkable feature is that some, but not all, experimentally-induced diseases will respond to synthetic antioxidants such as N,N'-diphenyl-*p*-phenylenediamine (D.P.P.D.) that are chemically unrelated either to selenium compounds or to vitamin E. It appears that, among the experimental diseases that do respond to synthetic antioxidants, a stress component has usually, if not invariably, been imposed by the ingestion of abnormally high intakes of polyunsaturated fats in the diet. While relatively large amounts of vitamin E will normally exert a similar protective action against the overt effects of nutritional stress caused by high intakes of unsaturated fat, it is not entirely clear whether there is ever a complete absence of such effects in diets in which the vitamin appears to play some role other than that of an antioxidant. However, from *in vitro* and *in vivo* studies described in a series of recent papers, Green and his co-workers (*e.g.*, Green *et al.*, 1967) have concluded that lipid peroxidation, if it occurs to any significant extent in the tissue of the living animal, is not related to the primary physiological function of α-tocopherol. Rather, they believe that the effects of dietary fat stress in vitamin E-deficient animals are due to destruction of α-tocopherol in the diet or the gastrointestinal tract, or to an increased requirement for vitamin E for the metabolism of certain long-chain fatty acids. In contrast to the effects of vitamin E, selenium (with some reservations) appears to have little or no effect on myopathies produced by experimental diets containing added unsaturated fat.

Among other factors, succinoxidase inhibitors may play some part in selenium-responsive diseases of livestock (Cartan and Swingle, 1959). In this context, Roughan (1965), in New Zealand, has found that clovers are particularly rich in some succinoxidase inhibitor (or inhibitors) as compared with grasses.

At present, the physiological role of selenium remains obscure and is the subject of much debate. It has been shown (Bieri, 1959; Zalkin *et al.*, 1960) that, in some circumstances, selenium compounds may exert antioxidant effects in *in vitro* biological systems and one school of thought contends that the entire or major function of α-tocopherol, and possibly of selenium, resides in the protection against peroxidation that they confer on tissues and membranes by reason of their antioxidant properties (*e.g.* Tappel, 1965). Other groups, while conceding, at least for vitamin E, a non-specific effect against toxicities resulting from the ingestion of unsaturated fats, claim for the vitamin (or a derivative) and for selenium specific, although differing, functions in respiratory enzymes.

Approaches to the problem of the role of selenium (if any) in respiration, differ.

An American group (Schwarz, 1965), investigating the α-ketoglutarate oxidase system, has evolved the working hypothesis that, theoretically, α-tocopherol, sulphur amino acids and selenium could all be accommodated within that system and that selenium may be involved in the first part of the sequence, namely the decarboxylation reaction. In Britain, other work, summarized by Green *et al.* (1961), suggests that selenium may be concerned in the biosynthesis of ubiquinone (coenzyme Q), a benzoquinone derivative related to α-tocopherol and involved in the respiratory chain.

The use of radioisotope techniques, and the development of fluorimetric methods of great sensitivity for the estimation of minute amounts of selenium (Cousins, 1960; Grant, 1963; Watkinson, 1960, 1966), have greatly facilitated progress in the knowledge of selenium metabolism.

In the sheep, the main route of organic or inorganic selenium, orally ingested in amounts that are either therapeutic (Cousins and Cairney, 1961) or physiological (Butler and Peterson, 1961), is via the faeces. It appears that, in the gastrointestinal tract, selenium compounds are largely converted to insoluble forms that may include metallic selenides or elemental selenium. Such forms, when voided, are not readily available to pasture plants (Peterson and Spedding, 1963).

Kidney and liver are important sites of selenium storage in the sheep (Cousins and Cairney, 1961; Hartley, 1967). As a result of his studies with ^{75}Se, Wright (1965a) considers that the kidney and the endocrine system may be specially implicated as sites of action of selenium. Of two groups of animals drawn from a flock of selenium-responsive sheep, the more rapidly-growing animals accumulated much more radioselenium in kidneys and pituitary, but not in other tissues, than did the more slowly growing animals (Wright, 1965b). In contrast, Andrews *et al.* (1963) found that poorly grown cobalt-deficient sheep had a significantly higher concentration of *total* selenium in their kidneys than did their better-grown cobalt-supplemented flock mates. However, as pointed out by Wright (1965a), if it is assumed that cobalt has no direct effect on kidney selenium, a high concentration of total selenium is not necessarily incompatible with a low rate of turnover as measured by radioselenium.

The forms in which selenium may occur in the mammalian organism have been discussed by McConnell (1963). It appears that the element may exist in both protein-bound and non-protein-bound forms and evidence is adduced that part of the protein-bound selenium exists as selenocystine, the selenium analogue of cystine. McConnell and Roth (1962) consider that, of the subcellular fractions, the microsomes appear to be the initial site for incorporating selenium into protein. According to McConnell and Levy (1962), in the dog and rat, both the α- and the β-lipoproteins incorporate ^{75}Se with the greater percentage in the α-lipoprotein. Recent New Zealand work, however (Roffler, Sheila A., Allsop, T. F., Mouw, A. J. and Wright, E. W., in preparation) suggests that serum lipoproteins are not a major factor in selenium transport. A paper by Cummins and Martin (1967) now appears to have reopened the whole question of the nature of protein-bound selenium. These workers have produced strong evidence that, in the rabbit, there is not a pathway for the *in vivo* synthesis of selenocysteine nor for selenomethionine. Rather, the selenium-containing compounds associated with fractions containing cysteine or methionine appear to be nothing more than selenite bound to the sulphur compounds.

Chemically, selenium is closely related to sulphur, and to some extent the two elements appear to follow similar biochemical pathways. Rosenfeld and Beath (1964) have reviewed the literature on selenium and sulphur antagonisms in biological systems. Although there is considerable evidence that in some systems compounds of sulphur will inhibit the effects of selenium when the latter is present in abnormally high concentrations, there is, as yet, no clear indication that sulphur (or other elements) might play a decisive part in selenium deficiency conditions.

SELENIUM-RESPONSIVE DISEASES OF SHEEP AND CATTLE

Selenium-responsive Myopathies

Hartley (1953) and Hartley and Dodd (1957) described myopathies (white muscle disease, muscular dystrophy, "stiff lamb"

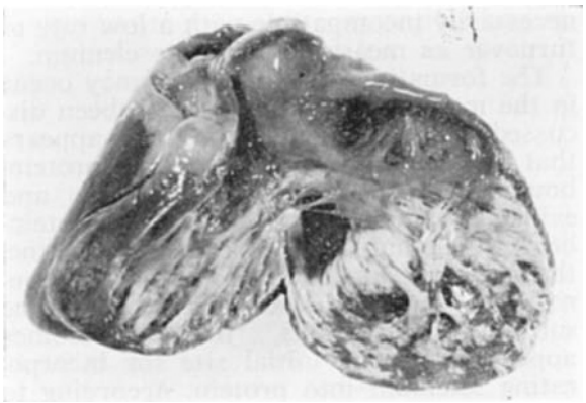

FIG. 1: *Selenium-responsive myopathy in lambs. Delayed white muscle disease with right ventricle showing extensive subendocardial pale areas of myonecrosis.*

disease) among farm animals in New Zealand. The latter workers concluded that the pathological features occurring in New Zealand livestock at pasture were indistinguishable from those found overseas in animals affected with a presumed deficiency of vitamin E, although they suggested that, in view of the supposedly high content of the vitamin in green feeds, complicating factors were probably present.

Much of the country where the selenium-responsive myopathies occur was, until recent years, largely undeveloped or run out. Following cultivation, seeding with improved pasture species and the liberal application of superphosphate, it now produces lush spring and autumn growth of grasses and clovers. Widespread outbreaks of selenium-responsive myopathies have usually been associated with seasons of luxuriant clover growth.

Two forms of selenium-responsive myopathy have been identified. These are commonly designated "congenital" and "delayed" white muscle disease (Hartley and Dodd, 1957; Grant *et al.*, 1960). (A further myopathy, seen in hoggets, will be mentioned later.) Both the congenital and the delayed forms may occur on the same property in the same season, and sometimes outbreaks of the delayed form are followed by selenium-responsive unthriftiness. Whereas both forms of white muscle disease are commonly encountered in lambs, only isolated cases of the delayed form have been seen in calves. It has been demonstrated (Drake *et al.*, 1960a; Hartley and Grant, 1961) that, in lambs, both forms can be controlled by the administration of selenium to the ewe prior to lambing and to the lamb at marking.

Congenital White Muscle Disease of Lambs

Affected lambs are either born dead, or may die suddenly after exertion (*e.g.*, suckling) within a few days of birth.

Post-mortem examination usually shows clear fluid and fibrin strands in body cavities, and a congested liver. The heart (Fig. 1) shows a mild focal to a most extensive diffuse greyish-white discoloration of the subendocardial myocardium. This lesion extends for only 1 mm into the myocardium and most commonly affects the right ventricle, although the other cavities may be involved. Skeletal musculature is rarely affected.

Microscopically, the initial lesion consists of large areas of non-inflammatory coagulative myonecrosis. This is superseded by lysis or calcification of the affected fibres, and replacement by macrophages and fibroblasts.

Delayed White Muscle Disease of Lambs and Calves

This form occurs predominantly in lambs from 3 to 6 weeks of age but can occur in those aged from 1 week to 3 months. The few cases seen in calves have occurred at ages of between 1 and 4 months. Affected animals have a stiff stilted gait and an arched back, are disinclined to move, lose condition, become prostrate and die. When being driven, some with severe heart involvement die suddenly. All recently-affected animals have high serum glutamic-oxalacetic transaminase (SGOT) levels (Blincoe and Dye, 1958), and an increased excretion of urinary creatine. Myoglobinuria is rarely seen.

Post-mortem examination shows a bilaterally symmetrical, focal or diffuse, yellowish-grey discoloration of several or many skeletal muscles. Cardiac lesions are not always present but, when they are, are similar to those seen in the congenital form of white muscle disease.

Microscopically, the skeletal lesions consist of extensive areas of non-inflammatory coagulative myonecrosis. This is followed

by lysis or calcification of affected fibres and invasion by macrophages and, if the animal survives long enough, muscle fibre regeneration.

Selenium-responsive Infertility in Ewes

Selenium-responsive infertility tends to occur in those areas in which congenital white muscle disease is found. Not infrequently, both entities occur on the same property in the same season (Grant *et al.*, 1960). In affected areas, lambing percentage (at marking) may be as low as 25% on some properties. The affected ewes may be of any age and are usually in fair to good condition at mating. Although they apparently conceive, many fail to produce a lamb. The cause of the infertility is embryonic death (Fig. 2) at about 3 to 4 weeks post conception (Hartley, 1963).

It has been shown that the embryonic mortality can be prevented by the administration of selenium to the ewe just prior to mating (Hartley, 1963). In extreme cases, lambing percentages were increased from 25% to 90% and from 80% to 120%. Although no experimental evidence is so far available, calving percentages for cattle grazing with sheep experiencing selenium-responsive infertility appear satisfactory.

Selenium-responsive Unthriftiness of Sheep and Cattle

Selenium-responsive unthriftiness is probably the most widespread and economically important of all the selenium-responsive diseases of New Zealand livestock. It occurs on improved properties, and is commonly associated with the liberal application of superphosphate and seasons of lush pasture growth. However, clover dominance is not a necessary prerequisite.

Sheep

Selenium-responsive unthriftiness in sheep varies from subclinical inability to maintain optimum growth rate (McLean *et al.*, 1959) to clinical unthriftiness which may, in bad seasons, lead to a heavy mortality (Drake *et al.*, 1960b). It occurs in all ages of sheep but is usually most severe in lambs and hoggets. Affected lambs may

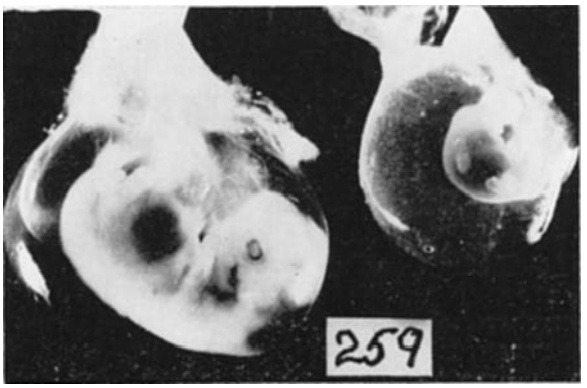

Fig. 2: *Selenium-responsive infertility. Ewe 30 days pregnant at slaughter. One twin viable, the other dead and undergoing resorption.*

apparently thrive for 2 to 3 months. Some may then show reduced weight gain. Others stop eating, stop growing, lose weight, become dejected, and die. Diarrhoea is not a constant feature but may occur if the condition is associated with endoparasitism. The fleece is harsh and dry. There is no increase in SGOT levels. The only post-mortem findings are non-specific advanced emaciation and osteoporosis. No characteristic microscopic lesions are apparent.

McLean *et al.* (1963) have described a further specific selenium-responsive syndrome in lactating ewes in Canterbury, characterized by rapid loss in condition and scouring in association with heavy parasitic infestation.

Extensive trials on pumice and sand country have shown that selenium will prevent or cure this type of unthriftiness in lambs and hoggets (Drake *et al.*, 1960b; Hartley and Grant, 1961). Treated animals produce up to 30% more wool than do those affected with unthriftiness and there is a suggestion that selenium may result in increased wool production by apparently thrifty adult sheep on properties experiencing selenium-responsive unthriftiness in young stock.

Cattle

Selenium-responsive unthriftiness can occur in all ages of dairy and beef cattle, particularly in the autumn and winter months (Hartley and Grant, 1961). It varies from a subclinical growth deficit to a syndrome characterized by a sudden and rapid-

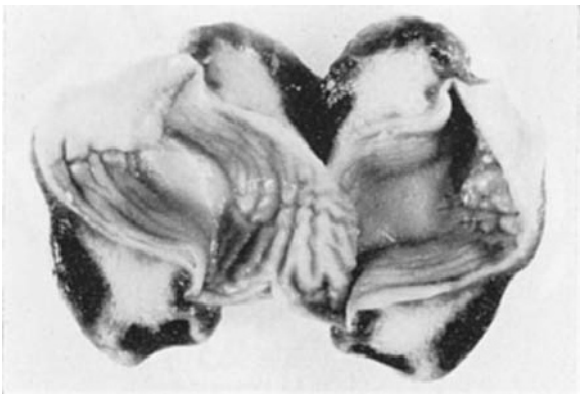

FIG. 3: *Selenium-responsive myopathy in chicks. Gizzard showing a large pale area of necrosis of the musculature.*

ly progressive loss of condition usually associated with a profuse diarrhoea and, sometimes, considerable mortality. Occasionally, severe outbreaks occur in adult cattle.

Trials with beef cattle on pumice soils have shown that selenium will prevent or cure this entity (Jolly, 1960; Hartley, unpublished), and Wilson (1964) has reported weight responses in dairy calves given a mineral supplement containing selenium.

PERIODONTAL DISEASE OF EWES

What now appears to be the same entity was first described in New Zealand by Salisbury *et al.* (1953), and subsequently by Hart and MacKinnon (1958) and MacKinnon (1959).

Not uncommonly, in both Islands the disease occurs in areas or on properties where other selenium-responsive diseases have been diagnosed. It is seen in ewes 3 to 5 years of age, and causes loss of condition resulting from difficulty in mastication. It is characterized by loosening and shedding of permanent premolars and molars, and sometimes also of incisors, in association with gingival hyperplasia, resorption and replacement fibrosis of alveolar bone, alveolar infection, and bony exostoses on the adjacent part of the mandible or maxilla (MacKinnon, 1959; Hartley, unpublished).

The association of periodontal disease with other selenium-responsive diseases, and its virtual disappearance on affected properties after selenium dosing, suggested that selenium might be implicated in the aetiology. Two long-term controlled selenium trials, one on a North Island coastal sand and the other in Southland, have shown that selenium administration will greatly reduce the incidence (Hartley, unpublished; B. W. Manktelow and C. E. Isaacs, pers. comm.). However, since treatment did not prevent the disease completely it seems that other factors are also involved.

SELENIUM-RESPONSIVE DISEASES OF POULTRY

Scott (1962) has pointed out that, whereas in chicks deprived of vitamin E three well-defined conditions appear, namely, encephalomalacia, exudative diathesis and white muscle disease, selenium appears to be concerned in the prevention of only the last two entities.

Outbreaks of poultry diseases now known to be selenium-responsive were first recorded in New Zealand by Thompson and Smith (1953). Those cases appeared to be associated with spoiled wheat and cod-liver oil and were preventable by vitamin E.

Selenium-responsive diseases of poultry are largely confined to the South Island and have been associated with the inclusion of South Island grain (low in selenium content) in the ration.

Two selenium-responsive conditions occur in chicks, a congenital myopathy (Salisbury *et al.*, 1962) and a delayed form of exudative diathesis (Hartley and Grant, 1961). The congenital myopathy is characterized by the birth of dead chicks, or weak chicks dying 3 to 4 days after hatching. Post-mortem examinations show extensive pale areas in the gizzard (Fig. 3), and sometimes also of hind limb skeletal musculature. Microscopically, these lesions consist of massive non-inflammatory coagulative myonecrosis.

Exudative diathesis is usually seen in chicks between 3 and 6 weeks of age. Clinically they are dejected, lose condition, show leg weakness and may become prostrate and die. Invariably they show a red or greenish-blue discoloration and swelling of the subcutaneous tissues, particularly under the wings and down the thighs. Post-mortem examination shows generalized subcutaneous blood-stained oedema and some-

times large pale areas of extensive interstitial oedema and congestion in the musculature together, in some cases, with non-inflammatory coagulative myonecrosis.

Controlled trials have shown that both the congenital and delayed forms can be prevented by selenium administration (Salisbury *et al.*, 1962).

SELENIUM-RESPONSIVE DISEASE OF PIGS

Workers in Scandinavia have reported a syndrome in pigs, called hepatosis diaetetica, which can be prevented by the administration of selenium (Grant, 1961). A condition indistinguishable from this has been recognized throughout New Zealand (Hartley and Grant, 1961). It is thought that its occurrence may be associated with the inclusion of South Island-grown grain, particularly spoiled wheat, in the diet.

Hepatosis diaetetica is seen in piglets principally between 6 and 14 weeks of age, and occurs either just prior to weaning or shortly after their transference to fattening pens. Clinical signs are seldom seen, animals usually being found dead.

Post-mortem lesions consist of copious quantities of clear straw-coloured fluid with strands of fibrin in body cavities. Subcutaneous and mesenteric oedema are sometimes present. The liver is enlarged and congested and exhibits, in peracute cases, a mosaic appearance consisting of groups of bright-red lobules (Fig. 4). In older-standing cases, there may also be fibrosis and fissures. In about half of the cases, the heart shows multiple minute white longitudinal streaks in the myocardium.

Microscopic lesions in the liver consist of focal multi-lobular areas of non-inflammatory hepatocellular necrosis, followed by parenchymal cell lysis and replacement haemorrhage. Non-inflammatory myonecrosis is seen in cardiac, and sometimes also in skeletal, musculature.

The possible involvement of polyunsaturated fats, low dietary protein and deficiencies of vitamin E and/or selenium in naturally-occurring cases of hepatosis diaetetica, has been discussed by Dodd (1966). Field evidence indicates that, when outbreaks have occurred and selenium has been given to survivors, deaths have ceased.

FIG. 4: *Hepatosis diaetetica. Liver showing widespread focal multi-lobular dark areas of hepatocellular necrosis and replacement haemorrhage.*

MISCELLANEOUS CONDITIONS THAT MAY BE SELENIUM-RESPONSIVE

MYOPATHY IN HOGGETS

This entity occurs principally in the southern half of the South Island, and may be found in 9- to 12-months-old hoggets that have been wintered for from 3 to 5 months on turnips or swedes. It tends to occur in seasons that are particularly cold and wet, and is precipitated by driving (Hartley and Dodd, 1957).

Clinical signs appear suddenly. There is rapidly developing listlessness, stiffness, inability to stand, prostration, and often death within 24 hours. Affected animals have high SGOT values and myoglobinuria.

Post-mortem changes are not always readily detectable in peracute cases. Affected musculature is paler than normal with a tendency to be dry and granular. Subcutaneous and body fat may be tinged pink. Cardiac lesions may be seen in chronic cases. Microscopic lesions consist of massive non-inflammatory coagulative skeletal myonecrosis.

Owing to the difficulty of predicting when this entity will occur, controlled trials have not so far succeeded in demonstrating a protective action of selenium. However, field reports indicate that, on properties where selenium is used as a presumed preventative, the disease has not recurred. One controlled trial carried out in 1954 showed that the myopathy could be prevented by α-tocopherol (Hartley and Dodd, 1957).

MYOPATHY IN DOGS

In the South Island, a congenital cardiac myopathy in a litter of newborn pups and a severe skeletal myopathy in adult dogs have been encountered (Manktelow, 1963). The macroscopic and microscopic lesions in both these entities closely resemble those seen in lambs.

MYOPATHY IN CATS

Gardner (1967) has reported a case of skeletal myonecrosis in a cat but it is not known whether this condition is selenium-responsive.

MYOPATHY AND STEATITIS IN FOALS

This specific entity is restricted to the North Island where it has been recognized on stud properties in Manawatu and Waikato (Hartley and Dodd, 1957). However, it seems to have occurred in areas where selenium-responsive diseases in sheep have not been observed.

The myopathy is seen in foals from 3 days to 5 months of age. Clinically, they show rapidly developing dejection, increased respiration, stiffness of gait, inability to lift their heads to suckle, prostration, and death within 1 to 7 days. Many foals show a painful swelling of the subcutaneous fat depots, particularly beneath the mane, and many also show excessive salivation associated with desquamation of the glossal epithelium. Myoglobinuria is usually present.

Post-mortem examination shows bilaterally symmetrical pallor of groups of skeletal muscles together with swelling and reddish-brown discoloration of subcutaneous and body fat. Microscopic changes in skeletal muscle are indistinguishable from those seen in delayed white muscle disease in lambs. The adipose tissue lesions consist of oedema and congestion with extensive neutrophile invasion followed by caseous necrosis and calcification.

This entity is suspected to be selenium-responsive on account of the myopathy and the fact that reports from affected properties indicate that since selenium has been used routinely as a preventative, the disease has not recurred. Nevertheless, its occurrence in areas where other animals are not apparently affected by selenium-responsive conditions leaves the question open.

DISTRIBUTION OF SELENIUM-RESPONSIVE CONDITIONS IN SHEEP AND CATTLE AND SOIL CLASSIFICATION

Congenital and delayed forms of white muscle disease in lambs may occur within a restricted area of pumice soils in the centre of the North Island and, sporadically, over much of the South Island, particularly on the stony and silty soils of the Canterbury Plains. On a few properties where the disease has occurred in lambs, the delayed form has been recognized among beef calves also.

Robertson and During (1961) have discussed the results of a Dominion-wide survey carried out by the Department of Agriculture to ascertain the distribution of selenium-responsive unthriftiness in lambs. Of trials on 274 different properties, carried out in the second season of the survey (1959–60), there were statistically significant responses on 14% of the North Island properties investigated and on 43% of those in the South Island. The map (Fig. 5), which is an adaptation of that prepared by Robertson and During (1961) and which shows the distribution of liveweight responses to selenium, is based on the results of some 700 trials carried out over three seasons.

In the North Island, the most consistent and marked responses were obtained on soils derived from recent ash showers of the Rotorua-Taupo area, on coastal sands from Wanganui to Paekakariki, and on light stony soils in Horowhenua, Hawke's Bay and Wairarapa. However, responses were not obtained on all pumice ash shower soils nor on all coastal sands. Thus, on extensive areas of pumice soils along the east coast from Whakatane to Napier, and in the King Country and South Waikato, no benefit was obtained from selenium. Similarly, no significant responses occurred on coastal sands extending along the west coast southward to Taranaki. In North Auckland, from Waikato southward to Wanganui, and from Cape Runaway southward along the east coast to Wellington, selenium deficiency, if present, appears to be rare. For some areas, notably in the South Auckland and mid-Hawke's Bay district, sufficient evidence is, at present, lacking.

In the South Island, marked responses to selenium were obtained on the Moutere

FIG. 5: *Liveweight responses of lambs to selenium. Selenium-deficient areas.*

soils of Nelson, on some areas in the Marlborough Sounds, and on predominantly alluvial soils of mid- and South Canterbury, Otago and Southland. Results of trials in Westland, parts of the Marlborough Sounds, North Canterbury and Banks Peninsula have so far been too few to permit appraisement.

Lamb weight-response results, summarized in terms of soil groups, were kindly provided by C. During (pers. comm.), and are as follows:

Response	*Soils*
None expected	Yellow-brown earths and yellow-grey earths (North Island). Most yellow-brown loams. Some yellow-brown pumice soils.
Very slight*	Yellow-brown loams (Tirau Suite).
Slight	Some brown-grey earths.
Marked	*North Island:* Coarse yellow-brown pumice soils. Coastal sands, Manawatu. Some light stony soils derived from old river terraces. *South Island:* Yellow-grey earths. Yellow-grey earths transitional to yellow-brown earths. Yellow-brown earths of the Uplands. Some Southern yellow-brown earths. Many recent soils (rainfall <60 in.).

*(Or response doubtful—see later).

The map (Fig. 5) should, of course, be interpreted with caution. Undoubtedly, selenium-responsive unthriftiness will occur, in some places, within areas delineated as showing a nil response. Thus, current investigations (F. van der Elst, pers. comm.) indicate weight responses of lambs and calves to selenium on peat soils in the Waikato and Hauraki Plains areas, respectively. Also, not all farms within the areas delineated as showing a marked response will be selenium-deficient. For example, in Southland during the 1959–60 season, growth rates were significantly increased in only 12 out of 20 trials carried out on farms situated within the area of "marked response" (Andrews, 1960).

So far as is known, farms on which the other selenium-responsive diseases of sheep or cattle may occur are found only within the areas indicative of selenium-responsive unthriftiness; that is, the map provides some indication of the distribution of selenium-responsive conditions generally.

SELENIUM CONCENTRATIONS IN SOILS, PLANTS AND ANIMALS

In this section, figures quoted for soils and pastures are on a dry-weight basis, and those for animal organs are on a wet-weight basis.

SOILS

Data on the selenium content of some mineral fertilizers, soil-forming rocks, and of samples from horizons of soil profiles of New Zealand soil groups, have been given in a series of papers by Wells (1966, 1967a, 1967b).

The average content of selenium in topsoils (0.60 ppm) is greater than that for parent rocks (0.42 ppm), indicating an accumulation of the element during soil formation. In general, Wells (1967b) found that selenium was very high (>1.5 ppm) or high (>0.90 ppm) in topsoils derived from andesitic or basaltic ashes or from argillite, low (<0.50 ppm) in those derived from mica schists or greywackes (excluding volcanic greywackes), and very low (<0.30 ppm) in most of those derived from granites or rhyolitic pumices.

Conditions inhibiting or favouring the leaching of selenium from soils have been discussed by Watkinson (1962) and by Wells (1967b). From analyses of soils from farms on which lamb weight responses had or had not been obtained, Watkinson (1962) concluded that a deficiency state might be encountered when the selenium content of soils was below 0.45 ppm.

PLANTS

At Wallaceville, Grant and Wright (unpublished) found that, if ^{75}Se is added to nutrient solutions in which clover plants are growing, the young growing leaves accumulate considerably greater amounts of radioactivity than do the mature leaves.

Differences in selenium content between different plant species have been reported by Davies and Watkinson (1966). For samples from plots topdressed with selenium they found that concentrations were greatest in browntop (*Agrostis tenuis* Sibth.) and least in white clover (*Trifolium repens* L.), with figures for cocksfoot (*Dactylis glomerata* L.) and ryegrass (*Lolium perenne* L.) falling between those extremes. However, perusal of their results suggests that, when selenium concentrations fall to very low levels (<0.01 ppm), differences between species tend to become negligible, a conclusion that receives independent support from other work (Grant unpublished).

In the light of later experience, some earlier Wallaceville figures (Andrews *et al.*, 1963) for selenium in pastures associated with an apparent mild selenium-responsive unthriftiness in sheep, appear suspiciously high. From two other more recent independent lines of evidence (Grant, unpublished; Andrews, Hogan and Grant, unpublished) indications now are that selenium-responsive unthriftiness is likely when pastures average less than 0.02 ppm of selenium. Figures for pastures grown on severely-deficient pumice soil reach very low levels (<0.01 ppm). It appears that the disease does not occur on pastures containing more than 0.03 ppm. These criteria are considerably lower than the figure (0.088 ppm) given by American workers (Burton *et al.*, 1962) for myopathy-producing hay, but not widely different from the critical level (0.03 ppm) suggested for myopathy-producing pastures in Western Australia (Gardiner *et al.*, 1962), and in fair agreement with figures for fodders producing white muscle disease, quoted by other overseas investigators (Oldfield *et al.*, 1963; Allaway *et al.*, 1966).

As compared with an Australian wheat sample (not associated with white muscle disease and exudative diathesis in poultry) which contained 0.15 ppm of selenium, South Island wheat samples (associated with those conditions) contained, on an average, 0.02 ppm (Salisbury *et al.*, 1962).

ANIMALS

Considerable New Zealand information is available concerning selenium concentrations in organs, tissues and fluids from normal animals, selenium-dosed animals and selenium-responsive animals (Cousins and Cairney, 1961; Andrews *et al.*, 1963; Hartley, 1967; Grant, unpublished). It is to be noted that selenium figures quoted by an American group (Oldfield *et al.*, 1963) for blood from sheep that developed white muscle disease on an alfalfa-oats diet are several times higher than New Zealand values for blood from pasture-fed lambs affected with selenium-responsive conditions (see later). On the other hand, where relevant, the New Zealand findings for white muscle disease in sheep are in broad agreement with those of other groups of workers (Burton *et al.*, 1962; Allaway *et al.*, 1966) in the United States.

Insofar as sheep are concerned, the following summarizes the main points that emerge from the New Zealand data.

(1) Highest concentrations of selenium are found in the kidney cortex, pituitary and adrenals. Concentrations in liver are intermediate. Muscle, bone, fat and blood are relatively low in selenium.

(2) Selenium administered at recommended rates does not raise selenium concentrations in food products from treated animals to undesirably high levels. Nevertheless, Hartley (1967) recommends that animals should not be killed for food within a week of receiving the last dose.

(3) Selenium concentrations in samples from animals affected with selenium-responsive conditions are considerably lower than those in corresponding samples from animals depastured in areas where selenium-responsive conditions do not occur.

Mean values reported by Hartley (1967) for liver, kidney cortex and blood from lambs with white muscle disease were 0.048 ppm, 0.24 ppm, and 0.016 μg/ml, respectively.

Mean selenium concentrations in liver and kidney cortex of hoggets affected with the myopathy associated with the feeding of turnips or swedes were 0.038 ppm and 0.40 ppm, respectively, (Hartley, 1967).

Figures for samples from young sheep showing weight responses to selenium have been reported (Andrews *et al.*, 1963; Hartley, 1967). Tentative indications from more recent experiments can be summarized as follows (Grant, unpublished):

	Selenium Content		
Degree of Unthriftiness	*Liver (ppm)*	*Kidney Cortex (ppm)*	*Blood (μg/ml)*
Marked	<0.02	<0.25	<0.004
Marginal	0.05	0.50	0.008
Normal	>0.10	>1.0	>0.010

Mean selenium concentrations in liver and kidney cortex of calves affected with white muscle disease were 0.035 ppm and 0.36 ppm, respectively (Hartley, 1967).

Analyses of milk samples drawn from an apparently normal dairy herd and from another herd grazing an area on which an apparent weight response to selenium had been obtained in calves, gave average selenium values of 0.006 μg/ml and 0.003 μg/ml, respectively (Grant, unpublished).

Hartley (1967) reported that selenium concentrations in liver and kidney cortex of pigs affected with hepatosis diaetetica averaged 0.047 ppm and 0.53 ppm, respectively. No normal figures were available for comparison, but the above values appeared similar to others (calculated on a dry weight basis) for hepatosis diaetetica in Sweden (Lindberg and Sirén, 1965).

General Considerations

Consideration of analytical and experimental data shows that, broadly, selenium concentrations in soils, pastures and bloods correlate reasonably closely with each other and with areas within which selenium weight responses would or would not be expected in lambs. However, there are some anomalies. For example, the high selenium content recorded by Wells (1967b) for Tirau silt loam (1.10 ppm) suggests either that the very slight lamb weight response, supposedly obtained on soils of the Tirau suite, was not, in fact, a true one, or that it was related to the few inches of Taupo pumice (0.14 ppm selenium) that, in part, covers the Tirau soils. Again, although no selenium responses have hitherto been obtained in North Auckland, the very low soil-selenium figure (0.20 ppm) for Te Kopuru sand in that province invites reinvestigation of possible animal responses, especially since the area involved is extensive (92,000 acres) and undergoing development.

The absence, in many cases, of white muscle disease and selenium-responsive infertility in areas experiencing selenium-responsive unthriftiness suggests that factors additional to low selenium intake may be concerned in the aetiology of those conditions. While it may ultimately prove that the form or degree of severity of enzootic selenium-responsive conditions in grazing animals can be influenced in that way the present writers consider that the weight of evidence supports the idea that, primarily, the diseases concerned have their genesis in low concentrations of selenium in soils and pastures.

DIAGNOSTIC AIDS

It is evident that the estimation of selenium in soils or plants would have value as a means of surveying large tracts of land, parts of which might be deficient in terms of animal health. However, it is doubtful whether exclusive reliance could ever be placed on the interpretation of soil or even plant analyses, as a guide to the use of selenium on individual farms. More precise criteria, based on analyses of blood or organs, offer possibilities but, at present, chemical analyses have only limited diagnostic application.

Godwin and Fraser (1966), using lambs raised on an experimental selenium-deficient diet, have made the interesting observation that the deficient animals showed abnormal electrocardiograms. However, the use of the electrocardiograph as a diagnostic tool awaits investigation.

Several chemical techniques, based on estimation of creatine or measurements of enzyme activity, have been suggested for the diagnosis of myopathies. SGOT levels, although not pathognomonic, can help confirm a diagnosis of white muscle disease or hepatosis diaetetica. However, for those conditions, and for exudative diathesis in poultry, histopathology remains the basis of most laboratory diagnoses.

At present, no laboratory procedures are used routinely for the diagnosis of selenium-responsive unthriftiness or selenium-responsive infertility. Where feasible, controlled selenium-dosing trials on the farm are recommended.

CONTROL

Topdressing Experiments

Topdressing as a possible means of preventing selenium-responsive diseases has been under investigation for a number of years in New Zealand.

Grant (1965) compared the effects of topdressing pastures with sodium selenate and sodium selenite and concluded that use of the latter substance might be practicable provided rates did not exceed the equivalent of 1 oz selenium per acre.

Apart from a passing effect due to surface contamination, only negligible amounts are taken up by pasture plants if selenium is applied in an elemental form (Grant, 1965; Watkinson and Davies, 1967), and applications of insoluble inorganic salts of the element appear to offer no advantages over those of the soluble salt, sodium selenite (Watkinson and Davies, 1967). Applications of gypsum at 2 or 10 cwt per acre had no effect on the selenium content of pastures (Hartley, 1967).

Topdressing trials on coastal sand and on pumice soils with soluble selenium salts applied at rates of ¼ or 1 oz selenium per acre gave weight gain responses in lambs, over a 9-month period, similar to those obtained from 5 mg selenium given orally each month (Hartley, 1967).

High initial levels of pasture-associated selenium are reduced by about half if the selenium compound used is incorporated into, and applied as a "frit" (Watkinson and Davies, 1967) or a prill (Grant, unpublished). However, recent studies (Grant and Andrews, unpublished) suggest that a simple preparation of sodium selenite mixed with superphosphate may be the most practicable method of prevention if it can be confirmed that amounts equivalent to as little as ¼ oz selenium per acre will suffice for a 12-month period.

Because selenium in excess can be dangerous, trials on a farm scale, over several years, will be necessary before selenium topdressing can be considered for use in practice.

Direct Administration Experiments

Drake *et al.* (1960a) compared the effects of selenium and of α-tocopherol in the control of field outbreaks of white muscle disease in lambs, and concluded that, while selenium almost completely prevented the disease, α-tocopherol was only partially effective.

The effectiveness of various compounds in controlling selenium-responsive unthriftiness or infertility in sheep has been studied by Hartley (1967). A finding of theoretical interest was that neither the synthetic antioxidant ethoxyquin (Santoquin) nor vitamin E had any effect on the unthriftiness or infertility syndromes.

Results of experiments carried out to assess the smallest selenium doses that will remain effective over the longest possible intervals have been summarized by Hartley and Grant (1961).

Recommended Methods of Control

Doses for sheep are usually given by mouth and contain 1 to 5 mg selenium (as sodium selenite or selenate) according to the age of the animal or the nature of the condition. To prevent infertility and congenital white muscle disease, ewes are dosed twice, about a month before mating and a month before lambing. Outbreaks of delayed white muscle disease should be treated as soon as they are recognized. Selenium-responsive unthriftiness in lambs can be prevented by dosing at marking, and thereafter at intervals of 2 to 4 months or when sheep are yarded for routine management procedures.

For convenience, cattle doses are usually given subcutaneously, the amounts varying from 10 mg selenium for calves to up to 30 mg for adults. Intervals may be at 3 months or as indicated by circumstances. Since risk from overdosing is greater when selenium is given subcutaneously, special care is necessary to ensure that recommended dose rates are not exceeded.

For preventing selenium-responsive conditions in poultry or pigs, selenium-containing supplements are now commercially available. These, when incorporated into the ration according to the manufacturer's instructions, provide 0.15 ppm of added selenium.

A more detailed account of the treatment and control of selenium-responsive diseases is contained in the handbook *Diseases of Domestic Animals in New Zealand* (Technical Committee. New Zealand Veterinary Association, 1962).

CONCLUSION

Areas of selenium deficiency are widespread in New Zealand and control of selenium-responsive conditions is of considerable economic importance. Improved diagnostic aids may depend upon a greater understanding of the physiological function of selenium about which not much is yet known. Nevertheless, reasonably satisfactory control of all known selenium deficiency conditions appears to have been achieved.

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