Acta vet. scand 1996, *37*, 19-30.

Selenium and Fertility in Animals and Man – A Review

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Hansen, J. C. and Y. Deguchi: Selenium and fertility in animals and man. Acta vet. scand. 1996, 37, 19-30. – To evaluate the information on selenium with relation to fertility in animals and man the available literature was reviewed. Selenium is incorporated in the sperm mitochondria capsule and may thus affect the behavior and function of the spermazoon Se seems to be essential for normal spermatozoa development in both experimental animals and in livestock and probably also in humans Regarding selenium and female fertility only sparse information exists In experimental animals a low selenium level affects fertility in males, but little attention has been devoted to female reproductive performance, and the data are insufficient for conclusion In livestock numerous investigations have been performed and the effects of selenium supplementation often in combination with other antioxidants have been evaluated, but no valid conclusion can be drawn In general adequate nutritional supply will secure optimal reproduction in both males and females, while additional supplementation seems to have a negative effect

In humans contradictive information is found Both low and high sperm selenium concentrations are reported to have a negative influence on the number of spermatozoa and on the motility The optimal sperm selenium concentration waits to be defined Some evidence indicates that a metabolic defect in a selenium incorporation into sperm cells may be associated with human infertility. No human data relating selenium to female infertility were found

experiment; livestock; humans.

Introduction

During the last decennia selenium (Se) deficiency in livestock has been recognized as a problem in various areas of the world *(Lannek & Lindberg* 1975, *Nebbia* 1982). As a consequence addition of selenium to foodstuffs has been widely used to provide an adequate supply.

During the 1980s Se has been recognized as being essential to humans too and several syndromes have been described in animals and in humans *(Koller & Exon* 1986) and etiologically explained as either Se deficiency or toxicity. Furthermore a relative deficiency has been discussed in relation to cancer *(Salonen et al.* 1984), cardiovascular diseases *(Salonen* 1987), neural diseases *(Westermark* 1977), and rheumatoid arthritis *(Tarp et al.* 1989). Se-containing preparations are commercially available and self-medication is now widespread in many countries.

Due to the toxic properties of Se, even in low doses, risks connected with use or abuse should not be underestimated and adverse effects such as acute and chronic intoxications are described

in both humans and in animals (AACT 1984, *Hill et al.* 1984, *Hooper et al.* 1985).

Se accumulates in the mammalian testis to a higher extent than it does in other tissues and it influences spermatozoal motility *(Benard* 1979, *Hidiroglou* 1982, *Behne et al.* 1986). By supplementation of low doses of Se to Se deficient rats, *Behne & Höfer-Bosse* (1984) found indications of the existence of a mechanism in Se distribution which favors the supply of testis, while the glutathione peroxidase status has a secondary status. Thus it can be assumed that Se, besides its well-known effects on the oxidative defence system through its function in glutathione peroxidase, may play an essential role in fertility in animals and man. The purpose of this paper is to review the literature on this subject.

Experimental animals

Se is essential for the normal development of sperm cells. Spermatozoa of rats are rich in Se (approx. 30 μg/g), of which the main part is found in a cysteine-rich polypeptide localized in the sperm mitochondrial capsules, (the "mitochondrial capsula protein" (MCP)) *(Calvin et al.* 1981, 1987, *Wallace et al.* 1984).

Se is incorporated in MCP in the early steps of the spermatogenesis under hormonal control. *Behne et al.* (1984) described the fact that hypophysectomia lead to reduced sperm Se concentration and that the concentration was normalized by administration of LH and FSH. A function of Se in the Leydig cells was indicated as plasma testosterone, after stimulation by LH-RH or LH, was lower in Se deficient rats compared to control animals, while no difference in hypophyseal LH secretion could be observed after LH-RH stimulation. *Wu et al.* (1971, 1979) found normal epididymal epithelium in Se-deficient rats, while many undeveloped and degenerated spermatozoa could be found in the luminal epithelium. The motility of epididymal spermatozoa was found to be diminished compared to a normal function in animals with a dietary supply of 0.1 mg Se/kg, while vitamin E did not influence the motility in the Se-deficient animal.

Wu et al. (1971) also observed that supplementation of chromium (1 mg/kg) to Se-deficient rats stopped the spermiogenesis. This observation indicates that other essential trace elements may also influence the mammalian fertility.

A toxic effect on testicular function in rats continually supplemented with Se was described by *Nebbia et al.* (1987). 16 ppm of sodium selenite in the drinking water lead to testicular degeneration. Biochemical evidence of tissue damage (increased lactate-dehydrogenase activity) was demonstrated even at a dosage level of 4 ppm.

Wallace et al. (1983a,b, 1986) found Se to be essential for the fertility in male mice. In mice, as in rats, Se deficiency resulted in abnormal development and morphology of the sperm mitochondrial capsules, increasing in frequency through generations of Se-deficient animals. In mice *(Wallace et al.* 1983a) in contrast to rats *(Wu et al.* 1973) only a weak relation between decreased motility and morphological abnormalities has been observed. Second generation Se-deficient mice were found to have a reduced sperm count. The deficiency in mice, as in rats, is associated with the lack of the MCP-selenoprotein.

Most investigations into the relationship between selenium and fertility in experimental animals have concentrated on males. One study, however, indicated that short-term supplementation of Se by injections of sodium selenite for 2 to 3 days increased the mass of reproductive organs in female mice and increased the number of fetuses. Prolonged dosing for 20 to 130 days gave the reverse effect *(Euybov et al.* 1983).

Livestock

Male fertility

In boars, fed an extremely low Se diet (0.01 ppm) based upon corn and soybeans grown in the Se-poor areas of China. *Liu et al.* (1982) found a reduced number of sperms as well as a reduced number of live sperms and increased occurrence of defect heads and tails. These findings are in contrast to other studies performed by *Segerson et al.* (1981) and *Henson et al* (1983), in which the content of Se in the basic feed was 0.025 ppm and 0.05 ppm, respectively. In none of these studies did supplementary Se have any effect on reproductive performance. Normal reproduction was observed in boars given a diet containing 0.05 mg/kg Se, while retarded sexual development was observed when increasing the content to 0.15 and 0.3 mg/kg *(Henson et al.* 1983). Post mortem examinations revealed no differences between dosage groups with regard to weight of testis, number of sperms or to sperm morphology.

Heimann et al. (1984) found no abnormalities in spermatozoon related to Se concentration in 12 bulls with a mean (± SD) blood plasma Se concentration of 61 μg/l ± 22 and a total mean sperm Se concentration of 461 ± 223 μg/l.

Se seems to be essential for normal spermatozoal development in livestock, as in experimental animals. A negative effect will, however, only appear at an extremely low Se intake, and normally accepted standards seem sufficient to secure normal fertility. A moderately high supplementation may exert a negative effect. There is a lack of information for a definition of an optimal Se status with regard to male fertility.

Female fertility

Cattle: Most investigations into Se in relation to reproduction in cattle have been devoted to studies on the effect on retained placenta. The incidence in USA is indicated as being 10%, however, in some Se deficient areas it may be as high as 50% *(Harrison et al.* 1984). *Trinder et al.* (1969) were the first to suggest Se as an etiological factor as regards this condition, and were later supported by others *(Julien et al.* 1976, *Trinder et al.* 1973). *Harrison et al.* (1984), however, stressed that a concomitant supply of vitamin E was necessary. *Eger et al.* (1985) found that Se supply through injections of 2.3 to 23 mg Se/animal reduced the incidence of retained placenta, but also concluded that relatively low doses of 2.3 to 4.6 mg/animal were more effective than were higher doses. Also *Caufalik* (1985) reports that Se therapy (50 mg/animal) in combination with estradiol, vitamin A, D and E had a prophylactic effect. However, which of the components that was responsible for the positive effect was not revealed by the author.

Blom et al. (1984) found in a Danish investigation of heifers with an in general marginal Se deficient status that supplementary Se increased the incidence of retained placenta.

In the investigations where Se supplementation was found to decrease the incidence of retained placenta, the animals were in a condition of absolute or marginal Se-deficiency and probably also suffered from other kinds of nutritional unbalances. Thus *Hidiroglou et al.* (1987) found in herds with a relative high incidence of retained placenta (22.1%), and sufficient Se-supply that further supplementation did not influence the condition and concluded that retained placenta in cattle is not Se-responsive.

In Norway *Ropstad et al.* (1987) investigated 17 herds with normal reproductivity performance and 47 herds with abnormal. A considerable part of the herds had a marginal Se deficiency defined as blood Se concentrations below 50 ug/l. In herds with a high Se status increased time from calving to last insemination compared to herds with low Se status was found. No

differences according to general health conditions were observed between low and high Se status herds. Corresponding negative findings were observed by *Blom et al.* (1984) in a study of Se supplementation to 17 Danish herds. *Spears et al.* (1986) found that a combination therapy of Se and vitamin E to beef cattle in a condition of marginal Se deficiency did not influence conception rate or interval between calvings. It did, however, reduce mortality in the offspring. Also other studies have shown negative results of a combined Se vitamin E therapy on reproductive performance in cattle with sufficient Se supply *(Hidiroglou et al.* 1987, *Koppel et al.* 1984, *Stowe et al.* 1988).

Segerson & Libby (1982) observed in 41 charolais cows with a marginal Se deficiency status (mean blood serum Se concentration 23 μg/l) that a combination of injections of 40 mg Se and 544 IU α-tocopherol every 14 days did not influence fertility, but that the number of sperms per ovum was correlated to the Se status of the cows. The authors suggested that Se facilitates the intrauterine sperm transport.

A positive effect of Se on neonatal mortality in calves and on general reproductive performance was reported by *Sanders* (1984) based on an investigation of two low Se status herds (herd I: 150 cows with blood Se concentrations from 23 to 44 μg/l; heard II: 70 cows with a blood serum Se between 30 and 54 μg/l). They recommended oral supplementation as more effective than parenteral administration, a view also pointed out by *Hansen & Kristensen* (1979).

McClure et al. (1986) observed an increased conception rate after oral supplementation of Se to cows with a mean whole blood glutathione peroxidase activity below 70 units/g hemoglobin; also *Tasker et al.* (1987) have reported increased conception rate after injections of Se.

In a number of publications from East European countries it is reported that a mixed antioxidative therapy exerts a positive effect on cattle reproduction. Unfortunately most of these publications do not indicate Se status prior to treatment and it cannot be ascertained whether the positive finding is due to the effect of Se or to other antioxidants. The multifactorial cause-effect relationship was indicated by *Grace* (1988), who showed that high intake of molybdenum can reduce fertility in cows.

Regarding cows the literature indicates that only in cases of evident Se deficiency, probably in connection with other nutritional deficiencies and poor hygiene, Se supplementation in combination with vitamin E is of importance for the reproductive ability. In well-fed animals signs of Se deficiency are very rare and furthermore moderate supplementation may give rise to negative effects. It is thus recommended that Se supplementation is only used on with a well documented deficiency *(Blom et al.* 1984). In cattle a blood serum Se concentration below 50 μg/l has been regarded as an indication of deficiency.

Pigs: *Chavez & Patton* (1986) investigated the effect of administration of 3 mg Se and 408 I.U. d-α-tocopherol to sows 3 times during pregnancy as a supplement to a feed containing 0.1 mg/kg of Se. No effect was observed in blood concentrations of neither Se, vitamin E, nor the glutathione peroxidase activity. In spite of no observed biochemical effects treatment improved litter size and birth weight. Neonatal mortality too was reduced in the treated group compared to controls. On the basis of these findings *Chavez & Patton* (1986) recommend, supplementation to sows of both Se and vitamin E beyond the recommended nutrition standards of 0.1 mg/kg of Se and 15 IU/kg of vitamin E. The documentation for this recommendation seems, however, to be weak and insufficient.

Jensen et al. (1984) found that single injections of 0.05 mg/kg of Se, as sodium selenite to 350 sows and gilts did not influence litter size and

neonatal mortality nor could any influence on the estrus cycle be demonstrated.

A report on positive effects of Se supplementation is given by *Momcilo et al.* (1987), who found increased litter size and slaughter weight in sows followed through 2 generations and supplied with 0.1 ppm Se in the feed compared to sows on a 0.03 ppm diet. In a Polish study *(Wandurski* 1988) better effect of vitamin E therapy (single injection of 0.6 g vitamin E) on fertility was found compared to a combination therapy of 0.376 g vitamin E and 5.5 mg sodium selenite per animal. This study had no control animals and the basic Se status was not indicated.

It may be concluded that it is not a documented fact that supplementation with Se alone or in combination with other antioxidants has any beneficial effect on reproduction in sows when recognized dietary standards are fulfilled.

Sheep: Intervention trials have shown that orally administrated Se is effective in reducing incidence of infertility in ewes and in increasing number of born lambs *(Hartley et al.* 1961, *Andrews et al.* 1968). *Segerson & Ganapathy* (1979) found that Se supplementation increased the uterine contraction thereby increasing the chance of fertilization. *Hartley* (1963) regarded Se deficiency as a cause of early embryo mortality (3-4 weeks of pregnancy).

Vipond (1984) reported that dosing to ewes of 5 mg Se together with other minerals and vitamins 2 weeks before mating had no effect on reproduction independent of the pre-dosing Se status evaluated by erythrocyte GSH-Px activity. Also *Kott et al* (1983) found no effect of injection of 4 mg of Se monthly during pregnancy with regard to number of lambs born. However, a combined Se vitamin E therapy increased the survival of lambs significantly. *Euybov et al.* (1983) reported that optimal dosing of sodium selenite to ewes (without actually defining what optimal means) increased the mass and volume of reproductive organs, increased fertility and number of live born lambs and birth weight. *Patkowska-Sokola* (1984) also reported positive effect on fertility, number of lambs born, and reduced mortality of lambs when the ewes were treated with injections of 5 mg Se as sodium selenite 4 weeks before mating and 8 mg 4 weeks before parturition. These animals had been grazing on sulfate-rich soils.

On the basis of the existing literature the effects of Se supplementation seem to be more effective in ewes than in dairy cows; this may be due to the fact that either the Se requirements in dairy cows have become more accurately defined or that cattle when compared to sheep are less sensitive to Se deficiency *(Grace* 1988). Otherwise in ewes as in cows the effect of Se on reproductive performance seems to be non-specific and probably related to the nutritional status. It seems advisable to establish the selenium status of the animals before a supplementation programme is implemented *(Van Ryssen et al.* 1992).

Horses: *Monroe et al.* (1988) did not find any effect of injections of 2.5 mg Se/45 kg to 8 pregnant mares compared to 8 control mares with regard to conception rate, gestational length, hormonal status, number of liveborn foals, stillborn foals, aborted foals, number of agalactia in mares, or retained placentas. Neither could *Taylor et al.* (1985) find any improvement in reproduction of pony mares as a result of Se supplementation.

Poultry: Reduction in egg production and increased embryonal mortality related to Se deficiencies has been observed in White Leghorn hens fed a 0.03 mg/kg Se diet without supplement of vitamin E *(Cantor & Scott* 1974). Both effects were restored to normal by adding sodium selenite in a concentration of 0.1 mg/kg. *Latshaw et al.* (1977) and *Combs & Scott* (1979) showed that a minimum of 0.05 mg/kg feed is required to maintain normal egg produc-

tion in hens, while Se concentrations below 0.1 mg/kg lead to reduced activity of GSH-Px and reduced hatching of eggs.

Petersen & Jensen (1984) investigated the effect on hens of a Se supplementation of 0.1 mg/kg to a basal diet containing 0.1 to 0.2 mg/kg. No effects were observed on number and weight of eggs, on fertility of eggs or percent of eggs hatched. Furthermore, no influence on mortality of hens and chickens was observed. The Se concentrations in eggs was increased from 0.13 to 0.19 mg/kg (yolk + white). A negative effect of Se supplementation in turkeys was observed by *Høj* (1983), who found reduced fertility in animals fed diets containing 0.32 and 0.47 mg/kg compared to a control group on a diet with Se concentration of 0.2 mg/kg. No reports have shown that Se deficiency influences male reproduction in poultry *(Combs & Combs* 1986).

In poultry Se is essential to maintain normal egg production and high hatchability of eggs. A dietary concentration of 0.1 mg/kg seems necessary to hens and 0.2 mg/kg to turkeys. A concentration of 0.3 mg/kg or more may have negative effects.

Fur animals: Injections of 0.3 mg Se to bitches of the blue fox, according to *Jørgensen et al* (1987), have been shown to be without effect on fertility, number of liveborn whelps, whelp mortality, and on the incidence of endometritis. No influence on GSH-Px activity was found, which could indicate that the animals, prior to therapy, were in Se balance and thus excreted the single parenteral dose quickly without any biochemical effects. *Kuliev* (1984) found that intravenous injection of 0.1 mg Se/kg as sodium selenite to nutria every month from birth increased the weight of ovaria, the number of follicles and corpora lutea. Unfortunately this publication provides no information on basic Se status in the animals.

Humans

For approximately 30 years it has been known that Se is essential to the spermiogenesis in experimental animals. In spite of this knowledge the interest in Se in relation to human fertility appeared only recently. *Bleau et al.* (1979) reported a mean normal Se sperm concentration of 190 μg/l and found high concentrations related to low sperm motility and reduced number of live spermatozoa. The authors suggested that Se might be involved in certain cases of human infertility. In a later investigation *(Bleau et al.* 1984) of 125 men from childless couples a mean seminal Se concentration of 71.3 ± 29.7 μg/l (range 7 –230 μg/l) was found. More than 85% of the total semen Se was found in the seminal plasma. A significant positive correlation between spermcount and sperm Se concentration was found. Motility was found to be highest when the seminal concentration was between 50 and 69 μg/l. When concentrations were below or above this interval motility was decreased and the incidence of asthenospermia high. On the basis of these results *Bleau et al.* (1984) suggest a seminal Se concentration between 40 and 70 μg/l to be optimal. When seminal concentrations were above 80 μg/l they observed a high abortion rate and signs of ovarial dysfunction in women, based upon the assumption that husband and wife normally have the same intake of Se from diet and environment.

In a methodological study of trace element determination in seminal plasma and spermatozoa *Pleban & Mei* (1983) found in men admitted to a fertility clinic seminal Se plasma concentrations from 21 to 191 μg/l and from 0.51 to 4.63 μg/l in spermatozoa. *Saaranen et al.* (1986) found in a similar group of 70 Finnish men, a mean concentration in seminal fluid of 33.4 ± 14.1 μg/l. This was less than half the level detected in blood serum, which was 78.2 ± 9.9 μg/l. *Suistomaa et al.* (1987) have re-

ported a spermatozoal concentration of 1.70 ± 0.1 μg/g in a pooled sample. These results are in agreement with the findings of *Bleau et al.* (1984), but are considerably lower than those originally reported by *Bleau et al.* (1979), where the mean sperm concentration was reported to be 190 μg/l. In the later findings they reported a seminal concentration of 80 μg/l or more having a negative effect. The early report certainly indicates too high a concentration level, which might be a result of a methodological error, however, the possibility of differences in the intake of Se between the populations cannot be excluded.

Takasaki et al. (1987a,b) determined Se concentrations in seminal fluid, seminal plasma and spermatozoa in 32 healthy fertile men and in 73 infertile (62 had oligozoospermia and or asthenospermia, 11 had azoospermia). No differences among the groups were seen as regards total sperm and seminal plasma Se concentrations. In seminal fluid the mean concentration was 80.1 ± 21.6 μg/l in the fertile group v.s. 77.1 ± 25.2 μg/l in the infertile group, and the seminal plasma concentrations were 70.4 ± 18.6 and 69.5 ± 21.9 μg/l respectively. In the spermatozoa the mean concentration in the fertile group was significantly lower compared to the infertile group (12.7 ± 70 $\mu g/10^8$ cells versus 29.7 ± 23.4 $\mu g/10^8$ cells). In contrast to this *Vanha-Perttula et al* (1988) did not find any differences between Se concentrations in spermatozoa from fertile (1.8 ± 0.8 μg Se/g d.w.) and from infertile men (1.3 ± 0.6 μg Se/g d.w.). *Takasaki et al.* (1987a,b) reported a positive significant correlation between seminal plasma concentration and spermatozoal density while a negative correlation was observed between spermatozoal Se concentration and density. Also the percentage of mobile spermatozoa was negatively correlated to the seminal plasma concentration. The authors suggested a connection between a high spermatozoal Se concentration and male infertility and suggested that Se exerts a negative effect on sperm motility and on spermiogenesis.

The results by *Takasaki et al.* (1987a,b) do not agree with the assumption made by *Bleau et al.* (1984) that a sperm concentration between 40 to 80 μg/l is optimal as both most fertile and infertile men in the Japanese study were found to be within this interval. On the other hand the possibility that a low Se intake per se might influence fertility negatively cannot be excluded, thus *MacPherson et al* (1994) found that a supplement of 100 μg Se to young infertile men with documented low dietary selenium intake increased sperm mobility significantly compared to a placebo group.

Roy et al. (1990) found no significant correlation between Se level in the seminal plasma and sperm count or motility. However, in view of the known poor correlation of these semen parameters with the incidence of pregnancy the authors state that assessment of the fertilizing potential of normospermic ejaculates with low selenium concentration is warranted.

An interesting feature of the results reported by *Takasaki et al.* (1987a,b) is that the spermatozoal Se concentration in all fertile men investigated was below 30 $ng/10^8$ cells, while one third of the infertile men had a higher cell concentration. As no difference between the 2 groups was found neither between full sperm nor seminal plasma concentrations, it may be assumed that the finding of high spermatozoal concentrations in some infertile men could be due to a defect in incorporation of Se into the MCP during spermatogenesis. Thus a high Se content, per se, is not necessarily the cause of infertility, but could be an indicator of a metabolic dysfunction being the primary causal factor in some types of infertility, since *Takasaki et al* (1989) also observed increased Se content in spermatozoa from fertile men after denaturation (of whole semen) by heat.

In areas without reported Se deficiency the mean seminal Se concentration is reported to be between 70-80 μg/l. Low as well as high Se concentrations in human sperm have been related to infertility. Higher spermatozoan Se concentrations have been found in some infertile men compared to fertile, which may indicate that a defect in Se incorporation in the sperm cells may be involved in some types of human infertility. From the existing literature no conclusions can be drawn, and more research on the role of selenium in human fertility seems to be needed.

Conclusions

The essential function of Se as regards to mammalian male reproduction is well-documented with regard to experimental animals, and livestock. Se has an essential role as a component of a selenoprotein in the sperm mitochondria capsula (MCP). Se deficiency leads to deterioration of spermiogenesis and to decreased sperm motility. However, it seems not to influence the ability of the individual spermatozoa to fertilize the ova. In females Se does not seem to influence reproduction in a specific way, but should be looked upon as a nutritional factor, among many others, which may influence dietary status, and, through this, health and reproduction.

In experimental animals and in livestock supplied with Se in amounts commonly accepted as being adequate further supply will not improve the reproductive conditions. Overdosing even at a moderate level has proved to have negative effects.

The need for dietary Se supplementation seems to be much more well-defined for experimental animals and livestock than it is for humans. The diversity of human recommendations found in literature should probably be explained through the fact that, contrary to animals, human dietary patterns vary to a great extent. As a consequence it may be assumed that also the need for supplements of antioxidants will vary both qualitatively and quantitatively. Furthermore, humans might be occupationally exposed to pro-oxidative components, which will increase the need for antioxidants. With regard to humans it seems likely that a defect incorporation of Se in sperm cells is a characteristic of some forms of male infertility.

There is a need for undertaking studies both in animals and humans to elucidate the relationship between dietary intake, optimal Se status and seminal (spermatozoal) concentration. There is also a strong need for a definition of a spermatozoal Se concentration, which is optimal for spermatogenesis and sperm motility taking into account various noxious environmental conditions. Finally there is a need for a further investigation as to whether high spermatozoal Se concentrations in some infertile men can be due to a defect in synthesis of polypeptides in the sperm mitochondria.

Acknowledgement

This work has been financially supported by Pharma-Nord, Vejle, Denmark.

References

Anonymous Toxicity with superpotent selenium. (American Academy of Clinical Toxicology). Vet Hum. Toxicol 1984, *26,* 527.

Andrews ED, Hartley WJ, Grant AB Selenium responsive diseases of animals in New Zealand. N.Z. Vet. J. 1968, *16,* 3-17

Behne D, Höfer-Bosse T Effects of a low selenium status on the distribution and retention of selenium in rat J Nutr 1984, *114,* 1289-1296

Behne D, Höfer-Bosse T, Elger W Interrelations between selenium and hormones in the male reproductive system (abstr.) Third International Symposium on Selenium in Biology and Medicine 28/5-2/6 1984, Beijing

Behne D, Duh M, Elger, W Selenium content and glutathione peroxidase activity in the testis of the maturing rat J. Nutr 1986, *116,* 1442-1447.

Bernard P Contribution á l'etude par autoradiographie macroscopique du metabolisme de de-rivés mineraux du soufre et du selenium chez differentes especes animales. (Contribution to the studies of the metabolism of mineral compounds of sulphur and selenium in different animal species by macroscopic autoradiography) Thése de Doctorat Ecole Nationale Veterinaire de Toulose, 1979.

Bleau G, Lemarbre J, Faucher G, Roberts KD, Chapdelaine A · Semen selenium and human fertility. Fertl. Steril 1984, *42,* 890-894.

Bleau G, Bousquet D, Clement M, Jean Y, Roberts KD, Chapdelaine A Selenium in human semen (abstr.) Fertility and Sterility 1979, *32,* 246-247

Blom JY, Thode-Jensen P, Sørensen JT, Østergaard V Forsøg med selenbehandling af kælvekvier på græs (Selenium treatment of grazing heifers). (In Danish) Dansk Vet. Tidsskr. 1984, *67,* 524-530.

Calvin HI, Grosshans K, Musicant-Shikora SR, Turner SI A developmental study of rat sperm and testis selenoproteins. J. Reprod. Fert. 1987, *81,* 1-11

Calvin HI, Cooper GW, Wallace E Evidence that selenium in rat sperm is accociated with a cysteine-rich structural protein of the mitochondrial capsules. Gamete Res. 1981, *4,* 139-149

Cantor AH, Scott ML The effect of selenium in the hen's diet on egg production hatchability, performance of progeny and selenium concentrations in eggs. Poultry Sci 1974, *53,* 1870-1879.

Chavez ER, Patton KL Response to injectable selenium and vitamin E on reproductive performance of sows receiving a standard commercial diet. Can J. Anim Sci 1986, *66,* 1075-1085

Combs GF jr, Scott ML The selenium needs of laying and breeding hens Poultry Sci. 1979, *58,* 871-884

Combs GF jr, Combs Stephanie B The Role of Selenium in Nutrition Academic Press 1986.

Coufalik V Die Prophylaxe von Retentio Secundinarum beim Rind (Prophyloxis of retained placenta in cattle). Tierarztliche Umshau 1985, *40,* 124-130.

Eger S, Drori D, Kadori I, Miller N, Schindler H Effects of selenium and vitamin E on incidence of retained placenta. J. Dairy Sci 1985, *68,* 2119-2122.

Euybov IZ, Shirinov NM, Rzaev RI Effect of selenium on reproductive organs and fertility of animals. (In Russian) Trudy Azerbaizhanskogo Nauchno-issledova-til'shogo Instituta Veterinarii 1983, *28,* 103-105.

Grace ND. Recent developments in trace elements in animal production. Proc. Austr. Soc. Animal Production 1988, *17,* 42-46

Hansen JC, Kristensen P The kinetics of ^{75}Se-selenium in relation to dose and mode of administration to mice J. Nutr. 1979, *109,* 1223-1233.

Harrison JH, Hancock DD, Conrad HR Vitamin E and selenium for reproduction of the dairy cow. J. Dairy Sci 1984, *67,* 123-132.

Hartley WJ Selenium and ewe fertility Proc N.Z Soc Anim Prod 1963, *23,* 20-27.

Hartley WJ, Grant AB A review of selenium responsive decreases in New Zealand livestock. Federation Proc 1961, *20,* 679-688.

Heimann ED, Smith MF, Morris JS, Gall TJ, Elmore RG, Morrow RE Relationships among spermatozoal abnormalities and the selenium concentration of blood plasma, semen, and reproductive tissues in young bulls Animal Reproduction Science 1984, *7,* 315-321.

Henson HC, Kattesh HG, Hitchcock JP, Kincaid JA The effects of dietary selenium on growth and selected reproductive parameters of young boars Anim. Prod. 1983, *37,* 401-407.

Hidiroglou M Selenium in the ruminant genital system and mammary glands A review. Ann. Rech. Vet. 1982, *13,* 133-141

Hidiroglou M, McAllister AJ, Williams CJ. Prepartum supplementation of selenium and vitamin E to dairy cows· Assessment of selenium and reproductive performance J. Dairy Sci 1987, *70,* 1281-1288.

Hill J, Allison F, Halpin C An episode of acute selenium toxicity in a commercial piggery. Aust Vet J. 1984, *62,* 207-209.

Hooper SA, Greig A, McMurray CH Selenium poisoning in lambs. Vet Res 1985, *116,* 569-571

Høj F Selen i æglægningsfoder til avlskalkuner. Linieafprøvning af kalkuner (Selenium in feed for breeding turkeys) Meddelelse fra Statens Husdyrbrugsforsøg No. 509, 1983, 4 pp.

Jensen AM, Jensen PT, Winter K, Jensen P, Skov Jensen EW Effect on perinatal mortality of a single selenium injection to sows and gilts Acta vet. scand 1984, *25,* 436-444

Julien WE, Conrad HR, Jones JE, Moxon AL Selenium and vitamin E and incidence of retained placenta in parturient dairy cows J. Dairy Sci. 1976, *59,* 1954-1960.

Jørgensen M, Henriksen P, Brandt A Blood selenium dependent glutathione peroxidase activity related to endometritis in blue fox (Alopex lagopus). Sciencifur 1987, *11,* 70-72

Koller LD, Exon JH The two faces of selenium deficiency and toxicity are similar in animals and man Can J Vet. Res 1986, *50,* 297-306.

Koppel LC, Ingraham RH, Morgan EB, Dixon MJ, Zeringue L, Wilson D, Babcock DK. Selenium concentrations in feeds and effects of treating pregnant Holstein cows with selenium and vitamin E on blood selenium values and reproductive performance. Amer J vet. Res 1984, *45,* 691-694.

Kott RW, Ruttle JL, Southward GM Effect of vitamin E and selenium injections on reproduction and preweaning lamb survival in ewes consuming diets marginally deficient in selenium J Anim Sci 1983, *57,* 553-558.

Kuliev GK Effect of selenium on the growth and reproduction of nutria (In Russian with English summary) Selskok-hozyaistvennay Biologiya 1984, *10,* 121-122

Lannek N, Lindberg P Vitamin E and selenium deficiencies of domestic animals Adv Vet Sci Comp Med 1975, *19,* 127-164

Latshaw JD, Ort JF, Diesem CD The selenium requirements of the hens and effects of a defiency Poultry Sci 1977, *56,* 1876-1881

Liu CH, Chen YM, Zhang JZ, Huang MY, Su Q, Lu ZH, Yin RX, Shao GZ, Feng D, Zheng PL Preliminary studies of influence of selenium deficiency to the developments of genital organs and spermatogeneses in young boars Acta Vet Zoo Tech Sinica 1982, *13,* 73-77

MacPherson A, Scott R, Yates R The effect of selenium supplementation in sub-fertile males In. Anke M, Meissner D, Mills, CF (eds.) Trace Elements in Man and Animals – TEMA8, 1995 566-569

McClure TJ, Eamens GJ, Healy PJ Improved fertility in dairy cows after treatment with selenium pellets. Austr. Vet J 1986, *63,* 144-146

Momcilo M, Velickovski S, Ilic V, Radetic P Growth and reproductive performance in pigs fed a diet low in selenium 38th Annual Meeting of the European Association for Animal Production, Lisboa, Portugal 28/9-1/10-1987 Commissions on cattle production, sheep and goat production, pig production and horse production 1987, Vol 2 , 1238-1239

Monroe JL, Cross DL, Hudson LW, Hendricks DM, Kennedy SW, Bridges jr WC Effect of selenium and endophyte-contaminated fescue on performance and reproduction mares J. Equine Vet Sci 1988, *8,* 148-153.

Nebbia C, Brando CE, Burdino E, Rasero R, Valenza F, Ausio R, Ugazio G Effects of the chronic administration of sodium selenite on rats testes Res Common. Chem Pathol Pharmacol 1987, *58,* 183-197.

Nebbia C Il selenio in medicina veterinaria (Selenium in veterinary medicine) Riv Zoot. Vet. 1982, *10,* 246-278

Patkowska-Sokola B Wplyw seleninu sodowego na wskaźniki rozrodu u owiec. (Effect of sodium selenite on reproduction in sheep) *Zeszyty Naukowe Akademii Rolnic zej we Wroclawiu* (1984), *144,* 31-37 [Pl, en, ru, 12 ref]

Petersen EE, Jensen JF Virkning af tilskud af selen til konsumægs- og rugeægsproducerende høners foder (Effect of selenium supplementation to laying hens). Beretning fra Statens Husdyrbrugsforsøg No 562, 1984, 51 pp.

Pleban PA, Mei D-S Trace elements in human seminal plasma and spermatozoa Clin Chem Acta 1983, *133,* 43-50

Ropstad E, Øvernes G, Refdal, A Selenium in Norwegian dairy herds related to reproductive and health performance Acta Agric Scand 1987, *37,* 397-405

Roy AC, Karunanithy R, Ratnam SS Lack of correlation of selenium level in human semen with sperm count/motility Arch Androl 1990, *25,* 59-62

Salonen JT, Alfthan G, Huttunen JK, Puska P Association between serum selenium and the risk of cancer Amer J Epidemiol 1984, *120,* 342-349.

Salonen JT Selenium in ischaemic heart disease Int J. Epidemiol 1987, *16,* 323-328

Sanders DE Use of selenium in problem cattle herds Modern Vet Pract. 1984, *65,* 136-138.

Segerson EC, Libby DW Ova fertilization and sperm number per fertilized ovarium for selenium and vitamin E treated charolais cattle Theriogenology 1982, *17,* 333-341

Segerson EC, Ganapathy SN Fertility of ova in ewes receiving selenium and vitamin E supplementation J. Anim Sci 1979, *49,* 335-340

Segerson EC, Getz WR, Johnson BH Selenium and reproductive function in boars fed a low selenium diet J Anim Sci. 1981, *53,* 1360-1367

Spears JW, Harvey RW, Segerson EC Effects of mar-

ginal selenium deficiency and winter protein supplementation on growth, reproduction and selenium status of beefcattle. J. Anim. Sci 1986, *63,* 586-594

Stowe HD, Thomas JW, Johnson T, Marteniuk JV, Morrow DA, Ullerey DE Responses of dairy cattle to long-term and short-term supplementation with oral selenium and vitamin E J Dairy Sci. 1988, *71,* 1830-1839

Suistomaa U, Saaranen M, Vanha-Perttula T Determination of selenium in human spermatozoa and prostasomes using base digestion and electrothermal atomic absorption spectrophotometry Clin Chim Acta 1987, *168,* 323-328

Saaranen M, Suistomaa U, Kantola M, Remes E, VanhaPerttula T Selenium in reproductive organs, seminal fluid and serum of men and bulls Human Reproduction 1986, *1,* 61-64

Takasaki N, Tonami H, Shimizu A, Ueno N, Ogita T, Miyazaki S, Deguchi Y, Ogata A Dansei-funinshou to seieki chuu selen ni tsuite (Semen selenium in male infertility) Jap. J Fert Ster 1987a, *32,* 345-351

Takasaki N, Tonami H, Shimizu A, Ueno N, Ogita T, Okada S, Miyazaki S Semen selenium in male infertility Bulletin of the Osaka Medical School 1987b, *33-1,* 87-96

Takasaki N, Shimizu A, Tonami H, Ueno N, Deguchi Y, Ogata A Seishou selen no seishi nai ikou (Tranfer into sperm of seminal plasma selenium) Medicine and Biology 1989, *118,* 241-243

Tarp U, Graudal H, Overvad K, Thorling EB, Hansen JC Selenium in Rheumatoid Arthritis A historical prospective approach J Trace Elem Electrolytes Health Dis 1989, *3,* 93-95

Tasker JB, Bewick TD, Clark RG, Fraser AJ Selenium response in dairy cattle New Zealand Vet. J. 1987, *35,* 130-140

Taylor MC, Loch WE, Ellersieck M Toxicity in pregnant pony mares grazing Kentucky – 31 fescue pastures Nutrition Reports Int. 1985, *31,* 787-795

Trinder N, Woodhouse CD, Renton CP The effect of vitamin E and selenium on the incidence of retained placenta in dairy cows Vet. Rec 1969, *85,* 550-553.

Trinder N, Hall RJ, Renton CP The relationship between intake of selenium and vitamin E on the incidence of retained placenta in dairy cows. Vet Rec 1973, *93,* 641-644.

Van Ryssen JB, Bradfield GD, Van Malsen S, De Villiers JF Response to selenium supplementation of sheep grazing cultivated pastures in the Natal Midlands J.S. Afr Vet Assoc. 1992, *63,* 148-55

Vanha-Perttula T, Kantola M, Suistomaa U, Saaranen M Comparison of glutathione peroxidase and selenium in human and bovine serum (abstr). Selenium in Biology and Medicine Fourth Int. Symp. Tubingen, 1988

Vipond JE Effects of a single oral dose of a commercial selenium cobalt and vitamin preparation on ewe fertility. Vet. Rec. 1984, *114,* 519-521.

Wallace E, Calvin HI, Cooper GW Progressive defects observed in mouse sperm during the course of three generations of selenium deficiency Gamete Res 1983a, *4,* 377-387.

Wallace E, Calvin HI, Ploetz K, Cooper GW Functional and developmental studies on the role of selenium in spermatogenesis In Combs GF jr, Spallholz JE, Levander OA, Oldfield JE (eds). Proc. Third Int Symp of Selenium in Biology and Medicine Avi Publ Co Westport Conn 1986

Wallace E, Wayne NJ, Calvin HI Functional and developmental studies on rat sperm selenoprotein (abstr) Third International Symposium on Selenium in Biol Med 28/5-2/6 1984, Beijing, China

Wallace E, Cooper GW, Calvin HI Effects of selenium deficiency on the shape and arrangement of rodent sperm mitochondria Gamete Res 1983b, *4,* 389-399

Wandurski A Wyniki zastosowania Evetselu u loch. (Results of Evetse application in sows) Medycyna Weterynaryjna 1988, *44,* 182-183.

Westermark T Selenium content of tissues in Finnish infants and adults with various diseases, and studies on the effects of selenium supplementation in neuronal lipofuscinosis patients Acta Pharmacol Toxicol. 1977, *41,* 121-128.

Wu SH, Oldfield JE, Whanger PD Effect of selenium, chromium and Vitamin-E on spermatogenesis (abstract). J Am Sci 1971, *33,* 273.

Wu SH, Oldfield JE, Whanger PD, Weswig PH Effect of selenium, vitamin E and antioxidants on testicular function in rats Biol Reprod 1973, *8,* 625-629.

Wu ASH, Oldfield JE, Shull LR, Cheeke PR · Specific effect of selenium deficiency on rat sperm. Biol. Reprod 1979, *20,* 793-798.

Sammendrag

Selen og fertilitet hos dyr og mennesker

Litteraturen er gennemgået for at vurdere viden om selen i relation til fertilitet hos dyr og mennesker
Selen inkorporeres i et cysteinrigt polypeptid lokaliseret i spermatozoers mitochondriekapsel. Selen må derfor antages at være essentiel for normal spermatogenese hos såvel forsøgsdyr, husdyr som hos mennesker. Der er derimod meget begrænset viden om selen i relation til hunlig fertilitet
Hos forsøgsdyr påvirker lav selenstatus hanlig fertilitet, mens der kun har været begrænset opmærksomhed om selenstatus og hunlig reproduktions adfærd, og data tillader ikke at drage konklusioner. Der er udført talrige undersøgelser på husdyr, hvor effekt af selen ofte er bedømt i kombination med andre antioxidanter, men definitive konklusioner kan ikke udledes. Generelt vil tilførsel i henhold til fodernormerne sikre optimal reproduktionsevne hos såvel han- som hundyr, mens ekstra tilskud synes at kunne medføre en negativ effekt.
Hos mennesker er der fundet modstridende resultater, idet såvel høje som lave spermakoncentrationer er fundet at have negativ indflydelse på antal af spermatozoer og på deres motilitet. Den optimale sperma selenkoncentration er endnu ikke defineret
Der er indikation for, at en metabolisk defekt i inkorporering af selen i spermatozoer kan relateres til human infertilitet. Der foreligger ingen data, der beskriver selen i relation til infertilitet hos kvinder.

(Accepted October 3, 1995)

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