STRESS AND FERTILITY. A REVIEW

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ABSTRACT

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The effect of both environmental and management related stressors on fertility is discussed. While environmental heat as a stressor is significant in disrupting normal reproductive cyclicity, management induced stress is becoming more important when related to the requirements of modern production methods. Deviations in hormonal patterns are noted, and the clinical manifestations brought about by these changes are described. Since reproduction is the ultimate measure of an animal's ability to adapt to an ever changing external milieu, as well as forming the basis of life-time productivity, research should be aimed at obtaining greater clarity of the hormonal interactions involved. The role of neurotransmitters in these physiological mechanisms should not be overlooked. Psychobiological studies must be extended so as to provide a positive input into management procedures that should be used in intensive production units for optimal fertility and productivity.

Nature's boldest experiment has perhaps been the placing of free ranging organisms in a constantly changing and often potentially hostile environment, thereby issuing a challenge not only to adapt and survive as individuals but also to retain the ability to procreate. Rock (1964) pointed out that reproduction was indeed the biological requisite for species survival, and it is now generally accepted that reproduction, as measured by the female's ability to conceive and produce viable offspring, is as good a measure as any of the animal's ability to adapt to a particular environment. As early as 1868, Darwin had in fact realised that animals which were confined were "eminently liable to suffer in their reproductive systems". In his study on factors influencing the breeding of captured wild animals, Hediger (1950) concluded that successful breeding was the mark of adequate captive conditions. While restriction of living space was a factor to consider, other external disturbances during the mating period which hinged on management procedures were equally important in achieving success. By careful attention to organisation as well as to the physiological and psychological "readiness" of the mated individuals, successful breeding can result.

Selye's (1936) original proposition of the effect of a stressor in setting off the sequence of body alarm, followed by the stage of resistance and culminating in the stage of exhaustion, still forms the basis for understanding and perhaps even explaining the delicate intricacies of the "stress syndrome". Stressors challenge the homeostasis of the animal, and the adaptation syndrome is the manifestation of the body's natural endeavour to maintain this homiostasis. Zoldag (1983) has discussed the modern perception of the complexities of stress in relation to reproductive activity in detail. The intricate interactions between the hypothalamus, hypophysis and adrenal, which form a neurohumoral axis modulated by the interspersion of the limbic system, come to the fore in the numerous manifestations of "stressors" on reproductive function.

While lower orders of life, such as Cladocera (Frey, 1982) and polyps (Sammarco, 1982), must, and do, adopt effective reproductive survival strategies to ensure continuation of the species, mammals are less able to control their reproductive destiny. This has been clearly shown in the steady roll-call to extinction of many species unable to adapt to changing enviromental or managemental circumstances in which they have found themselves. In the overall concept of animal husbandry, man plays a significant role in creating stress, but, perhaps of greater importance, he can provide the means to alleviate, remove or modify any potential stressor. That there is an urgent necessity to re-evaluate stress in farm animals has been clearly set out by Dantzer & Mormede (1983), who point out the need for a more integrated view of the stress reactions shown by farm animals.

In terms of modern production methods this call is perhaps long overdue, since the demands of managemental systems installed to increase production have often had adverse effects, especially when measured against reproductivity, with significant negative economic impact. The overall effect of stress on fertility in the various domestic species, has been well documented. Recent papers have set out the position in cattle (Collier, Beede, Thatcher, Israel & Wilcox, 1982; Lewis, Thatcher, Bliss, Drost & Collier, 1984; Marschang, 1973; Moberg, 1975; Monty & Wolff, 1974; Wagner, 1973; Zoldag, 1983); in pigs (Britt, Szarek & Levis, 1983; Hennessy & Williamson, 1984; Mercy & Godfrey, 1980) and in sheep (Brown & Harrison, 1984; Marschang, 1973). The effects of stress on reproduction in laboratory animals has also been recorded in detail (Clough, 1982). The value of taking note of these experiences with laboratory animals lies in the feedback to be gained from the management of controlled environments.

In all systems of management there are 2 groups of stressors, namely, environmental stress and management related stress (Moberg, 1975; Zoldag 1983). Environmental stress includes environmental temperature, either heat or cold, wind, and humidity. Management related stresses consist of animal density; handling procedures; movement of animals; intraspecies interaction and social status; interspecies interaction; psychological distress; noise and physical trauma. Single factors from each group, or combinations of such factors, can serve as stressors which can significantly challenge the homeostasis of the animal. The overall effect of this challenge will further depend on the *duration of the stimulus, and* its *intensity* or *strength*. As long as the stressful event remains a challenge, the animal will be under stress. The behavioral responses and physiological changes that follow on the challenge manifest themselves in various adverse ways as the effects of the stress.

In the reproductive process of any female animal taken from oestrus to parturition, the stage from oestrus to implantation appears to be the one most susceptible to the possible adverse effects of stress (Moberg, 1975). Stress on any female during pro-oestrus and oestrus, when the utero-hypothalamo-hypophysio-ovarian axis is delicately poised in an intricate negative feedback interchange associated with folliculogenesis and ovulation, has decidedly detrimental effects on subsequent reproductive events (Hennessy & Williamson, 1983; Marschang, 1973; Moberg, 1975; Monty & Wolff, 1974). The clinical manifestations of stress-effected oestrous cycles are essentially the same in all females, reflecting

as delayed ovulation or anovulation; cyctic ovarian degeneration; a shortened less intense oestrus; reduced conception rates; embryonic death, and irregular oestrous cycles. These deviations from the norm may follow on exposure to either environmental or managemental stressors.

The most important environmental stressor influencing reproductive performance is environmental heat (Britt *et al.,* 1983; Lewis *et al.,* 1984; Monty & Wolff, 1974). Cold conditions, on the other hand, appear to exert no significant effect (Collier *et al.,* 1982; Swierstra & Rahnefeld, 1972). One of the interesting features of environmental heat-induced effects on the reproductive system is the marked reduction in uterine blood flow (Brown & Harrison, 1984; Collier *et al.,* 1982). Depending on the stage of the reproductive cycle, of course, the influence will vary. At oestrus there will be, apart from increased intrauterine temperature, an effect on glandular activity as well as the nature of the glandular secretion which interfere with normal capacitation (Chang, 1966). Decreased uterine blood fow, acting in unison with altered hormonal profiles, also leads to a drop in the number of leucocytes in the lumen, and this contributes to a lowering of defence mechanisms. (Chang, 1966; Frank, Anderson, Smith, Whitmore & Gustafsson, 1983; Grandin, 1984). Increased uterine temperature, altered uterine environment, poor gamete quality and reduced immune status, acting alone or in combination, may all contribute to early embryonal death. Once implantation has occurred, the decrease in uterine blood flow that follows on protracted periods of increased environmental heat will cause impaired placental function, leading to restricted foetal growth. This shows up as lower birth masses and decreased offspring viability (Brown & Harrison, 1984; Lewis *et al.,* 1984; Marschang, 1973).

Grandin (1984) provides an excellent review of the various manifestations of stress induced by handling. He highlights such stressful situations as health-care procedures, isolation of animals from herdmates and rough handling during insemination, amongst others, all factors well known in animal husbandry, but often not put into correct perspective in terms of lowered reproductive performance. He accentuates the value of accustoming animals to routine handling procedures so as to minimize the deviant physiological reactions caused by stress. In looking at the effects of high ambient temperatures on the reproductive performance of gilts, Hennessy & Williamson (1984) also emphasize the significance of management procedures over and above possible environmental stressors in causing infertility. They point out that while "summer infertility" in sows is certainly a reality, the syndrome must also be considered within the context of management factors.

Holt (1962) and Wagner (1973) both refer to a long-recognized environmental stressor, movement. The positive effect of transport stress on oestrus provocation in pigs, particularly gilts, is well known. Movement of cattle, on the other hand, when measured against non-return rate to service, has an adverse effect on fertility. Apart from the physical stress of transport, the strangeness of the new environment plays an important part in altered adrenal function, and this is ultimately reflected in reduced fertility. Reproductive problems induced by movement can persist for periods of up to 2 months after transportation.

Modern trends in animal breeding infer a concentration of animals in a restricted space (Marchang, 1973), making environmental adjustments essential to ensure optimal productivity. Wagner (1973) refers to the effect of crowding in creating conditions of social stress which bring about unavoidable interaction between dominant and subordinate animals with its concomitant effect on reproductive efficiency. The intriguing phenomenon of the aperiodic mass migrations of the Scandinavian lemming which every 7–10 years desert overcrowded grazing grounds and living areas in a frenzied suicidal escape, has long fascinated researchers of stress (Rock, 1964; Andrews & Strohbehn, 1971). Interestingly enough, stressed individuals, unable to cope with the overcrowded conditions, showed enlarged adrenals and increased levels of corticoids, progesterone, oestrogen and androgens. The exceptions to the self-regulatory population control mechanism were small groups of dominant pregnant females which had near normal adrenal steroid levels, which were apparently unaffected by the population density stress, and which were destined to ensure the survival of the spesies.

While the importance of light:dark cycles in regulating reproductive events in horses and sheep is well known, light as a stressor has never been given serious thought. Clough (1982) reviewed the possible effects of light in terms of intensity, wavelength and photoperiod, mostly as applicable to laboratory animal management. It was interesting to note the vast difference in the intensity of natural light in bright sunlight versus overcast conditions. Personal observations on the suppressive effect of overcast weather on overt signs of oestrus in synchronized cows opens up an interesting area for investigation of light as a "stressor" on pineal activity.

In modern production systems, little attention is given to auditory stress and its possible effect on fertility. Singh & Rao (1970), however, reported the occurrence of polycystic ovaries in rats exposed to a prolonged period of auditory stress. While interspecies extrapolation is always dangerous, it may be expedient to note, this observation as production methods intensify to meet modern day demands.

While the effects of stressors are manifested in several distinct clinical syndromes in the female animal, the changes provoked in the male are clinically not so obvious and are outwardly far less dramatic. As regards the extent of their influence on the herd or flock, however, the picture can be quite devastating. The main manifestation is a significant drop in semen quality (Larsson & Einarsson, 1984; Marschang, 1973; Stone, 1981). Changes involve reduced sperm motility with a rise in the number of dead sperm, an increase in retained cytoplasmic droplets and heightened acrosome damage, all of which indicate some form of epididymal malfunction. Derangments of spermatogenesis occur on occasion, but are infrequent. Lack of, or apparent lack of, libido can be found to be due to various stressors, such as long spells of high environmental heat or the suppressive effects of a socially dominant male. In any investigation of stressor-induced infertility, therefore, the potential involvement of patho-physioligical changes in the male should not be overlooked.

It is abundantly clear that external stressors so influence the internal phsiological milieu that normal reproductive functions are often disrupted. Clinical manifestations can be clearly demonstrated. What then are the underlying mechanisms involved? Clearly the overriding effect is on the endocrine system, upsetting the delicately balanced hormonal interactions required to ensure optimal reproductive function. Stressors stimulate the exteroceptive sensory systems of the cortex as well as provoke afferent impulses from olfactory, optic and auditory sensory systems. These stimuli, together with interoceptive sensory impulses, are received by the limbic system which then serves to modulate hypothalamic

and hypophyseal function. Within the limbic system is a massive richness of interconnecting pathways which integrate circuits from the neocortex and convert them into the complex neurohumoral control of the activity of the endocrine system.

Several workers have demonstrated hormonal changes in both acutely and chronically "stressed" animals (Abilay, Johnson & Madan, 1974; Echternkamp, 1984; Hennessy & Williamson, 1983; Lewis *et al.*, 1984; Miller & Alliston, 1974). These changes include initial cortisol rise with subsequent depression, raised progesterone levels, changes in LH surge in terms of both LH peak as well as the time of the peak relative to the start of oestrus, changes in basal levels of LH, lowered FSH levels, raised PGFM levels, and increased ACTH levels. Furthermore, epinephrine and norepinephrine levels are also increased (Aguado & Ojeda, 1984; Blake, 1976). Recently, Przekop, Wolinska-Witort, Mateusiak, Sadowski & Domanski (1984), looking at the effect of stress on the oestrous cycle of the sheep, pointed out that levels of serotonin and β-endorphin had been shown to have an inhibitory effect on LH release.

Absence of a preovulatory surge of LH, a lowered peak, or a shift in the timing of the peak will all exert an influence on ovulation. If the LH peak is inadequate to provoke ovulation, cystic ovarian degeneration may follow (Hennessy & Williamson, 1983). Apart from the negative feedback effect of progesterone on LH release, increased levels of progesterone, probably of adrenal origin, will also affect endometrial function with concomitant changes in uterine milieu, potentially influencing gamete and zygote survival.

While the main emphasis of stressor effect appears to be on the hypophyseal-adrenal axis, Dantzer & Mormede (1983) point out that complex hormonal and neurotransmitter changes are occurring in other systems at the same time, which, while poorly understood at this stage, could play an important role in possible pathophysiological changes affecting fertility. Because of the clear influence of stressors on signal hormones of reproduction, some effect of stress on fertility is inescapable. The magnitude of this effect will naturally be determined by the summation of stressors, by their intensity and duration. From their first tenuous gasp, all forms of life will be subject to stressors which man can modify, alleviate or eliminate. In his paper on the limits to animal production, Blaxter (1979) expresses the optimistic viewpoint that man is much too sensible an animal to allow the outstripping of the resources of his earth to produce food. He will certainly have to bear in mind that, in terms of reproduction, adaptation to stress has its limitations. Strict selection methods can, and do, pay dividends in building up populations more able to resist the rigors of reproduction stressors (Brown & Nestor, 1974; Horst, 1983). Research efforts will have to be directed more intensely at unravelling the endocrinological mechanisms involved in the pathophysiology of reproduction. Furthermore, because of the ever-increasing intensification of animal production, management related stressors will have to be clearly delineated and studies on psychobiology greatly expanded. In this context, Wagner (1973) stated that, in striving for optimum fertility, first and foremost attention should be given to the animal's happiness and contentedness. While on first appearance this statement appears utterly simplistic, the depth of insight it projects sets the premise for the psychobiological input into modern production methods necessary to ensure optimal reproductivity, and hence productivity.

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