INTRODUCTION

For both scientific and commercial reasons there is an urgent need for informed discussion and further research on the relationship between stress and immune competence of cattle in feedlots. As the Australian feedlot industry is in a period of rapid growth, considerable attention is being given to issues of public concern such as waste management, odour, disease (including usage of antibiotic drugs) and animal welfare. The recent Report of the Senate Standing Committee on Rural and Regional Affairs entitled Beef Cattle Feedlots in Australia (1992), highlights the importance of these issues. Thus, the commercial viability of the Australian feedlot industry in the future will depend on researchers, and indeed the industry itself, satisfactorily addressing such issues. In the scientific context, there is a growing recognition of the nexus between the central nervous system, the endocrine system and the immune system (Moberg 1985). Impairment of immune competence as a consequence of stress should not be seen as a phenomenon restricted to cells or molecules of the immune system, rather as a problem for the whole animal, with neuroendocrine implications (Griffin 1989; Kelley and Dantzer 1990). Furthermore, there is an obvious link between stress, impaired immune competence and animal welfare. The relationship between stress and compromised immune competence therefore has important implications for the feedlot industry ranging from public perception/consumer resistance through to improved profitability associated with more efficient disease control.

Of course, the point should be made that the stress/immune competence interaction is an issue not only for the feedlot sector. The beef cattle industry has other forms of intensification such as grain supplementation in the paddock and “finishing” steers on irrigated, improved pastures. In these situations, during transportation and, indeed, in all other examples of intensification of livestock production systems, the link between animal stress and reduced immune competence is important.

In this paper we shall:
(a) briefly describe some of the important disease problems in feedlot cattle in Australia;
(b) provide some preliminary results of new research on stress in feedlot cattle;
(c) outline the research program on Animal Health and Welfare in the Cattle and Beef Industry Cooperative Research Centre (CRC).

DISEASE PROBLEMS IN FEEDLOT CATTLE IN AUSTRALIA

Because the feedlot sector is a relatively new sector of the beef industry in Australia there is very little relevant scientific literature available. Recently scientists from NSW Agriculture have been involved in a Survey of Extent and Causes of Illness in Feedlot Cattle and they are now carrying out an intensive clinical and epidemiological study of these diseases. The survey has drawn attention to several important issues. First, feedlot managers rated respiratory disease as the most important problem, followed by hoof

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problems, feed-related problems and "bulling", that is, buller steer syndrome. The direct costs of disease ranged from 3¢ to $6.81 per case (mean $1.78). These direct costs, however, represent only a fraction of the total cost of disease. Mr Rod Hadwen, General Manager of the feedlots operated by Australian Meat Holdings (Beef City Feedlot at Toowoomba) and former President of the Australian Lot Feeders’ Association (ALFA), maintains that bovine respiratory infection alone accounts for a 10% reduction in feedlot efficiency, or $50 per head of feedlot capacity. Thus, for a 25,000-head feedlot in Australia bovine respiratory disease causes an annual loss of income in excess of $1 million (R Hadwen, pers. comm.).

In the Survey, feedlot managers reported annual morbidity rates of 5.8 to 129.5 cases per 1,000 head (mean 57.9) and annual mortality rates of 1.1 to 13.7 per 1,000 head (mean 6.9). There was a significant negative correlation between clinical case rate and age. The highest prevalence of respiratory disease occurred within the first month after entering the feedlot, with respiratory infections being much greater in younger animals (two-tooth or less). These findings are consistent with reports in the literature for feedlots in the northern hemisphere (Brown 1968; Andrews 1976).

Preliminary findings from the detailed disease study indicate that Pasteurella hemolytica and P. multocida are frequently isolated from animals suffering respiratory disease, but Salmonellae, Haemophilus somnis and Actinobacillus pyogenes are also implicated. Notwithstanding the importance of bacterial infections in bovine respiratory disease, there is considerable evidence that bacterial infections frequently follow primary viral infections with organisms such as bovine respiratory syncitial virus, infectious bovine rhinotracheitis, bovine virus diarrhoea (pestivirus) and para-influenza type 3 and/or Mycoplasma spp. (Jensen 1968). Respiratory infections are also the major disease problem encountered in feedlots in North America where the bovine respiratory disease complex-exacerbated by transport stress-is known as “Shipping Fever”. A great deal of effort has gone into the development of vaccines and drugs to prevent or treat Shipping Fever in feeder cattle in the USA and Canada where very large quantities of antibiotic drugs are used both prophylactically and therapeutically (Jensen et al. 1976). Recognition of the risks associated with indiscriminate use of antibiotics is a relatively recent phenomenon. At a conference of feedlot veterinarians in the USA in 1967 one delegate stated in relation to respiratory infections:

"we do not really have a problem. All we have to do is put antibiotics in animal feed and we have no problem." (Reisinger 1968)

The world has changed since then! Antibiotic resistance in pathogenic microorganisms, consumer resistance to foodstuffs containing drug or chemical residues and the risk of embargoes on our exports mean that such attitudes now would attract universal condemnation.

The role of stress in diseases of feedlot cattle is well recognised but incompletely understood. Cattle entering feedlots may be stressed in various ways. For example, they may suffer social stress (overcrowding, disruption of stable social hierarchies by mixing mobs), temperature stress (heat, cold, humidity, wind chill) and transportation stress (overcrowding, deprivation of feed and water, lack of rest). One of the consequences of acute stress is that it causes an increase in circulating levels of glucocorticoid hormones which in turn result in reduced immunological competence (Griffin 1989). An example of the effect of transportation stress on immune parameters is shown in Table 1.
Effect of transportation on immunological/physiological parameters in Angus steers* (measurements made at time of unloading of shipped cattle)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
<th>Shipped</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes (μl⁻¹)</td>
<td>10,366</td>
<td>13,960</td>
</tr>
<tr>
<td>Lymphocytes (μl⁻¹)</td>
<td>2,572</td>
<td>6,099</td>
</tr>
<tr>
<td>Neutrophils (μl⁻¹)</td>
<td>200</td>
<td>840</td>
</tr>
<tr>
<td>Genic response to con A (cpm x 10³)</td>
<td>143</td>
<td>92</td>
</tr>
</tbody>
</table>

*from Blecha et al. (1984).

Low-grade, chronic stress probably also impairs immunological competence, but the nature of this relationship is not as well described.

Chronic, although slight, elevation of glucocorticoid concentration in blood has been shown to be associated with different housing conditions in intensively managed pigs (Nett et al. 1984). There are many recent reviews (e.g., Khansari et al. 1990) dealing with the interactions between hormones produced by the neuroendocrine system and cellular activity and cytokine production by the immune system. Table 2 summarises the interactions which could be relevant to the effects of stress on the immune system of cattle. Some hormones are known to enhance rather than suppress the immune system, but it is not known whether low levels of these hormones may interfere in some way with immunity.

Table 2 | Neurohormones which have immunomodulatory properties*

<table>
<thead>
<tr>
<th>Neurohormones</th>
<th>Action</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucocorticoids</td>
<td>S</td>
<td>Antibody production, NK activity, cytokine production</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>S</td>
<td>Lymphocyte proliferation to mitogen</td>
</tr>
<tr>
<td>Endorphin</td>
<td>E/S</td>
<td>Antibody synthesis, macrophage activation, T-cell activation</td>
</tr>
<tr>
<td>ACTH</td>
<td>E/S</td>
<td>Cytokine production, NK activity, macrophage activation</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>E</td>
<td>Antibody synthesis, macrophage activation, IL-2 production</td>
</tr>
<tr>
<td>Somatostatin</td>
<td>S/E</td>
<td>PFC, mitogen response</td>
</tr>
<tr>
<td>VIP</td>
<td>S/E</td>
<td>Cytokine production</td>
</tr>
<tr>
<td>Oxytocin, ADH</td>
<td>E</td>
<td>T-cell proliferation</td>
</tr>
</tbody>
</table>

S = suppression, E = enhancement
* Table modified from Khansari et al. (1990)
Because of the involvement of neuroendocrine factors in the immune system it is not surprising that links are evident between the behaviour of animals and their immune responses (e.g., Fell et al. 1991, Gates et al. 1992). Further research is needed into the effects of stress on the behaviour of feedlot cattle and the way this may be related to the immune competence of these animals. Moberg (1987) proposed that suppression of the immune system was one of the main criteria to be used in a model for assessing the impact of behavioural stress on domestic animals.

The generalised reduction in immune incompetence associated with stress, plus the continuous close contact between animals in trucks and in the feedlot, lead to an increased risk of infectious diseases. Additionally, of course, pre-slaughter stress is of great importance to the cattle industry because of its deleterious effects on meat quality (e.g., dark-cutting meat).

**RESEARCH IN PROGRESS**

Very little research has been done in Australia on animal stress in feedlots particularly with regard to its links with disease. The only kind of stress which has received attention is heat stress—or what Young (1992) has termed excessive heat load. Literature about this problem in the Australian context has been reviewed recently (Blackshaw and Blackshaw 1991; Young 1992; Blackshaw 1992) and it is discussed elsewhere in this Symposium by Professor Young. There is no mention of the implications for immune competence or disease status in the cattle.

A rise in circulating levels of glucocorticoid hormones has been shown to occur in heat-stressed dairy cows (Wise et al. 1988). However, research by the Queensland Department of Primary Industries (Clarke 1993 and personal communication) on the plasma cortisol concentration of Brahman cross feedlot steers in central Queensland has shown no difference between those provided with complete shade and those with no shade during the hottest time of the year. This could be taken to indicate that these particular cattle, which are known for their heat tolerance, were not stressed, but further work is needed.

Some effects of climate variables on the behaviour of feedlot cattle are reported elsewhere in this Symposium by Fell and Clarke. This research was in fact initiated by the Australian Lot Feeders’ Association, with financial support from the Meat Research Corporation, and is now included within the ambit of the Cattle and Beef Industry CRC. From a consideration of behavioural responses there is no clear indication of climatic stress affecting cattle in those feedlots. Cattle do show the expected adaptive responses to hotter or cooler weather and to such factors as relative humidity and rainfall. At this stage, the observations being made do not provide any information about possible links between immune system parameters and cattle behaviour.

The main aim of this work in progress is to determine the production and welfare effects on British breed cattle of providing shade in feedlot pens in different climatic regions from northern Victoria to southern Queensland. The results of this study will be available by the end of July 1993. In the course of the study, we have recorded some changes in respiration rate associated with hot weather. The natural adaptive response of cattle to heat is to increase respiration rate at first (from normal values of 50-80/min to around 120-140/min in a few individuals which we have observed), that is, a shift to rapid, shallow breathing. Subsequent adaptation, as heat load continues, is a shift to slower, deeper breathing (which we have observed in a few animals at around 70-110/min). From health data collected so far, there is no indication that the health of these animals has been compromised in any way. The overall incidence of sick animals has
<1% and there have been no mortalities reported in the shade project at this stage. There is no provision for physiological measurements other than the stockman’s assessment of respiration rate and there are no hormone measurements being made in this study.

In a new project (also funded by the Meat Research Corporation) we will be looking at the possibility of improving the resistance of cattle to stress by various nutritional, behaviour and vaccination treatments (a package to be known as pre-boosting) applied at the time of weaning. To date, one study has been conducted (Fell and Bertus to be published) of the changes in behaviour which occurred in calves kept in yards for 7 days immediately after weaning, that is, after separation from their mother. This has provided benchmark data on the behavioural reactions of young cattle to psychological stress which will be used as a guide to possible means of strengthening their resistance to future disease challenges by manipulating their immune system at this time.

THE HEALTH AND WELFARE RESEARCH PROGRAM IN THE CATTLE AND BEEF INDUSTRY CRC

The Program has five goals, listed below:

1. Develop vaccines against bovine respiratory disease caused by Pasteurella hemolytica and ‘pestivirus.
2. Reduction of antibiotic residues in beef.
3. Development of a panel of tests for quantitating immunological competence in cattle.
4. Identification of the specific stress factors which compromise immunological competence and development of procedures which ameliorate their effects.
5. Development of acceptable indices of animal welfare for the feedlot industry.

A major effort in the first three years of the CRC’s existence will be development of a novel composite vaccine to prevent bovine respiratory disease. A rationally attenuated, live P. hemolytica vaccine will be developed by deletion of the leukotoxin gene (lkt C) from the bacterial chromosome and re-introduction of a “toxoided” gene. This will be done using a plasmid vector system. The attenuated strain of P. hemolytica will be used as a live vaccine; additionally, a strong promoter will be inserted into the strain to provide a fermentation strain capable of producing large quantities of toxoided leukotoxin in vitro. In our Virology Laboratory monoclonal antibodies will be used to identify and select three strains of pestivirus for preparation of an Australian pestivirus vaccine. Genes coding for the Gp 53/55 envelope glycoproteins (protected antigens) will be cloned into a baculovirus vector. The two vaccines will be tested in combination, together with appropriate immunological adjuvants in weaner calves. A commercial veterinary vaccine manufacturer will be involved in testing and commercialisation of the vaccine.

A panel of clinical immunology tests will be developed for assessment of immunological competence of cattle. These tests will be directed at innate immunity (e.g., complement, lysozyme), immune induction (e.g., antigen-presenting cells, MHC Class II expression) and immune effector mechanisms (e.g., antibody responses, eosinophil numbers). These tests will be standardised and accredited. In a series of carefully controlled experiments immunological competence will be measured in cattle subjected to a number of stressors (individually and in combination). Thus the specific stressors (and interactions) responsible for impairment of immune competence will be identified. A schematic representation of the pathways involved in stress-immune function interactions is shown in Figure 1.
Experiments will be conducted in an attempt to ameliorate stress and the accompanying depression of immune competence. Three approaches will be used. Firstly, cattle will be immunised against stress-mediating hormones such as adrenocorticotrophic hormone (ACTH). Secondly, changes in management/ husbandry will be utilised to reduce stress. Thirdly, immunostimulating drugs will be used to non-specifically enhance parameters of immune defence.

Studies will be undertaken on behavioural physiology of cattle in order to identify indices for assessing welfare status. An arena test, recently developed for sheep, will be adapted to cattle to enable monitoring of the animal’s cognitive states. Ethograms (behavioural repertoires) will be developed for cattle in commercial feedlots and changes in adaptive behaviour will be measured. These new data will enable us to generate animal welfare indices.

REFERENCES

“Survey of Extent and Causes of Illness in Feedlot Cattle” (1992) NSW Agriculture, Orange, NSW.