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What is sickness motivation, and why does it matter?

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Introduction

For the swine industry, sick pigs are costly in terms of mortality, labour, veterinary and pharmacological inputs, and poor performance. In addition, animal health is a significant factor impacting animal welfare, due to suffering associated with injuries and disease. Husbandry standards are increasingly coming under scrutiny by retailers and the public. Effective health management practices for detection, management and prevention of illness and injury are well-recognized components of quality assurance programs, such as SWAP. Although there has been little investigation of sickness behavior specifically in swine, it is useful to examine knowledge emerging from basic science about how animals respond behaviourally to pain, injury and disease. These concepts suggest that understanding of sickness behavior can provide a new management tool and opportunities to enhance standard operating procedures for managing swine health.

What is "sickness behavior"?

During acute stages of illness, animals alter their behavior so that activity, social interactions, grooming, feeding and drinking are reduced, whereas huddling, shivering and resting increase. Swine producers and veterinarians recognize many of these changes as typical clinical signs of disease (Straw *et al*. 1999). In a pivotal review, Hart (1988) pointed out that these changes in behavior occur across a wide range of mammalian and non-mammalian species in response to a wide range of bacterial, viral and parasitic infections. Since evolution favours diversity, preservation of such a consistent response is unusual and suggestive of strong underlying biological advantages or selection pressures. Hart suggested that this "sickness behavior" is a component of a highly organized evolved strategy to combat infection, involving behavioral, immune and endocrine systems. Subsequent research in the interdisciplinary field of psychoneuroimmunology supports Hart's hypothesis, revealing that sickness behavior is mediated by pro-inflammatory cytokines, IL-1, IL-6 and TNFa, within specific sites of the brain. As part of the innate immune response, these cytokines are released by immune cells, such as macrophages, and can cross the blood-brain barrier. These cytokines are also produced directly in the central nervous system by glial cells in response to vagal nerve stimulation (Dantzer 2003).

Fever is an important component of the immune response to reduce pathogen proliferation (Kluger *et al*. 1975; Vaughn *et al*. 1980). However, mounting a fever is energetically expensive, requiring a 13% increase in metabolic rate for mammals to increase body temperature by 1°C. Hence, fever is maintained by drawing from the animal's energy reserves through glycogen and protein catabolism, but cannot be sustained without changes in behavior to reduce energy demands for other functions. In particular, slow wave sleep increases in association with onset of the febrile response (Toth *et al*. 1994), and enhanced sleep is associated with a more favourable prognosis and less severe clinical signs during bacterial infections in rabbits (Toth *et al*. 1993).

The fact that animals usually respond to illness and injury by reducing activity and increasing rest has traditionally been viewed as a consequence of debilitation. However, research with laboratory rodents indicates that responses to illness are more complex. Administration of the bacterial endotoxin lipopolysaccharide (LPS) induces a characteristic proinflammatory cytokine cascade, and sickness behavior, such as anorexia, thermoregulatory behavior, increased rest, and reduced activity. When LPS is administered to rats, the resulting sickness response causes rats to alter their dietary preferences from proteins towards carbohydrates (Aubert *et al*. 1995a). Furthermore, rats show reduced abilities to learn new tasks, but do not affect performance of tasks previously learned (Aubert *et al*. 1995b). Interestingly, gender differences exist since LPS reduces sexual behavior in female rats, but not in males (Yirmiya *et al*. 1995). Furthermore, the way in which sickness behavior is expressed is context-dependent. In behavior terms, this means that sickness can be viewed as a specific motivational state that competes for expression with other motivational states, such as fear, hunger or sex. When LPS is administered to lactating female mice, sickness behavior competes with maternal behavior. Nest building behavior, key component of maternal behavior in mice, is only performed when mice are at cool environmental temperatures, 6C versus 22C (Aubert *et al*. 1997a). Similarly, food-hoarding behavior by rats is significantly reduced in response to LPS challenge when food is freely available, but hoarding continues to be performed by rats that have been previously trained to work for a portion

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of their daily ration. This is interesting, since hoarding occurs when the rats are anorexic and hence, they are anticipating and responding to their future needs rather than immediate hunger (Aubert *et al*. 1997b).

In addition to changes in behavior due to activation of the immune response, some pathogens can affect the host's behavior directly. For example, toxoplasmosis causes increased restlessness and risk-taking behavior in rodents, which is believed to make them more vulnerable to predation by cats, the terminal host for this parasite (Klein 2003). Other researchers have also shown that some bacteria, such as *Campylobacter jejuni*, can stimulate the vagal nerve in rodents to produce behavioural responses such as increased anxiety without provoking clinical signs of infection or the classical cytokine cascade (Gakema et al. 2004).

What are the implications for how we manage sick pigs?

Sickness motivation in swine has important implications for diagnosis, treatment and prevention of disease. When unfamiliar hogs are mixed, shedding and transmission of *Salmonella cholerasuis* has been shown to occur within hours (Gray *et al*. 1996). Similarly, social stress has been shown to increase shedding of *Salmonella* by early-weaned pigs (Calloway *et al*. 2002). Although researchers have explored the effects of behavior on immune function, particularly stress and social behavior (Hessing *et al*. 1995; Tuchscherer *et al*. 1998), there are only a few detailed studies exploring how swine express sickness behavior. Administration of LPS causes dose-dependent increases in rest and decreases in feed intake, and profound anorexia is observed even when pigs have been deprived of feed for twelve hours (Warren *et al*. 1997). Vomiting, salivation and chewing have also been reported to increase in response to LPS (Girod *et al*. 2000). However, since LPS rapidly induces effects of acute systemic infection, the biological relevance to naturally occurring infections in commercial swine production is questionable.

Currently, my research group is using an ampicillin-induced diarrhea model to explore how weaner pigs alter their behavior during subclinical and clinical stages of infection (Millman *et al*. 2004). This model is also being used to explore how illness affects social interactions in groups of ill and healthy pigs. Interestingly, we found that the clinical and behavioural responses to a microflora shift depend on the social context. When weaned pigs are housed individually, our ampicillin model induces mild to moderate diarrhea for 24-48 hours, and pigs display increased rest and seek social contact at this time (Millman et al., 2006). Conversely, clinical signs of diarrhea were not observed when pigs were housed in groups of three familiar pigs and only one pig received the ampicillin treatment. In the group pens, the treated pig displayed more aggression towards his pen-mates and did not display increased rest (Colgoni et al., 2006). These results have important implications for detection of illness in group-housed swine, since social facilitation of behavior may impact the likelihood of clinical signs being detected.

Policy makers (Council of Europe Scientific Veterinary Committee 1997), industry quality assurance programs (Pork Check off Swine Welfare Assurance Program, p.32-33), and animal welfare certification protocols (Certified Humane) recommend the use of hospital pens for the care of ill and injured swine. However, there is scant information or guidance about how such facilities should be designed or managed. In a survey of 100 swine farms in Ontario, 70% of producers indicated that they used hospital pens, but when these responses were investigated further, few producers had designated infirmaries or standard operating procedures for the care of ill and injured pigs (Millman, Friendship & Dewey, unpublished data). Reasons for separating pigs into hospital pens varied, including infectious and non-infectious disease conditions, injuries and behavioral problems. The care provided for ill pigs once they were placed in hospital pens varied considerably, with inspection of animals in sick pens occurring once daily on one-third of the farms and twice daily on a further third of the farms. Sick pigs were treated with antimicrobials on 94% of the farms, and segregating ill pigs into hospital pens may facilitate identification and handling affected individuals. Conversely, on 5% of the farms, ill and injured pigs were segregated, but given no additional treatment or inspection. These results suggest that producers use hospital pens for convenience of handling and to minimize transmission of pathogens, but there is considerable scope for improvement in managing the recovery of ill and injured pigs.

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