

1 Broom, D.M. 2006. Behaviour and welfare in relation to pathology. *Appl. Anim. Behav.*  
2 *Sci.*, 97, 71-83.

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4 Pre-publication copy

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## **Behaviour and welfare in relation to pathology**

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### **Abstract**

16 Behaviour is an important way of adapting to disease for individuals and selective

17 pressures resulting from disease have had major consequences for the evolution of

18 behaviour. Behaviour, adrenal and other physiological responses, immunological

19 responses and brain activity all help in coping with disease. Health is an important part of

20 welfare and any pathology implies some degree of poor welfare. Sickness behaviour and

21 physiology are generally adaptive, involve interactions with the immune system and are

22 partly mediated by cytokines. Since, firstly, an understanding of some behaviour requires

23 knowledge of disease and, secondly, responses to disease and studies of brain and

24 behaviour are helping to increase understanding of systems for combating disease,

25 interdisciplinary co-operation is needed for the development of these areas of science.

1

2 **Keywords.** Pathology, health, welfare, abnormal behaviour, disease, brain, cytokine,  
3 infection, immune suppression, sickness, pleasure.

4

## 5 **1. Introduction**

6

7 The central topics to be considered in this paper are the ways in which behaviour, adrenal  
8 and other physiological responses, and brain activity change during disease. The first  
9 issues considered are some of the links between behaviour and health which have been  
10 reviewed in more detail elsewhere. There is confusion about the meaning of key  
11 concepts in the paper and their inter-relationships so ideas about these are presented and  
12 discussed. The various methods for coping with pathogens, in particular the role of  
13 cytokines and sickness behaviour, are reviewed. The interactions amongst the various  
14 responses and their consequences for welfare are also discussed.

## 15 **2. Some examples of links between behaviour and health**

16

17 There are many links between behaviour and health. Behaviour has an important role in  
18 the transmission of a wide variety of diseases. For some diseases, an aspect of the normal  
19 behaviour of an infected animal, for example mating, is necessary for effective  
20 transmission of the pathogen. In some other cases the behaviour may not be normal and  
21 pathogens and parasites change host behaviour so that transmission is more likely  
22 (Holmes and Bethel 1972). For example, fish with an eye fluke swim near the surface  
23 where the next host, gulls, may catch them (Crowden and Broom 1978). Many pathogens

1 depend for transmission upon the behaviour of a vector of a species different from the  
2 main host.

3

4 The changes in behaviour brought about by disease are used by veterinarians and medical  
5 doctors in the diagnosis of disease (Broom 1987, Fraser and Broom 1990). For example,  
6 a dog with abdominal pain may arch its back, sheep with foot-rot may kneel and a bull  
7 with traumatic reticulitis may walk with a characteristic stiff-legged gait. Some examples  
8 of changes in brain and behaviour associated with sickness or malaise are considered later  
9 in this paper.

10

11 Some behaviour has evolved because of selective pressures that are principally a  
12 consequence of those parasites and diseases that seriously reduce inclusive fitness. One  
13 example is preference for bright plumage during mate selection by female birds, because  
14 sick or parasitised males would often be less bright and are less suitable mates (Hamilton  
15 and Zuk 1984). Another example is behaviour which results from feelings of malaise and  
16 consequent inappetence, which allows energy to be retained for immune system function  
17 when fighting infection.

18

19

### 20 **3. How are the concepts of health, pathology and welfare inter-related?**

21 It is important that there should be a balanced view of the importance of the various  
22 components of the welfare of animals, including humans, but scientists from different  
23 backgrounds may differ in the emphasis which they place on the importance of health.

1 There is a tendency for ethologists to under-emphasise the health aspects of welfare and  
2 for veterinarians and human doctors to under-emphasise behavioural and brain function  
3 indicators of good or poor welfare. Psychiatrists and neurologists are aware that the brain  
4 has a key role in regulating most aspects of life but the dramatic interactions of the brain  
5 with disease control mechanisms in the body, studied by psychoneuro-endocrinologists,  
6 should be better known.

7

8 What is the health of an animal? The views of people differ in respect to the way in  
9 which they use the concept of health. For some, health in a farm animal refers solely to  
10 the impact of diseases that affect its potential for good production. For others, the main  
11 significance of animal health is related to the likelihood of zoonotic infection and  
12 transmission to humans. For a third group of people, health is a very wide term which  
13 refers to everything which could be good or bad in life? Do any of these views explain  
14 the meaning of health? For me, and I think for most people, health refers to the state of  
15 the body and brain in relation to the effects of pathogens, parasites, tissue damage or  
16 physiological disorder. Since all of these effects involve pathology, the health of an  
17 animal is its state as regards its attempts to cope with pathology (see next section, Broom  
18 2000, Broom and Kirkden 2004 for discussion). If the welfare of an individual is its state  
19 as regards its attempts to cope with its environment (Broom 1986) and pathology is one  
20 of the effects of environment, then it is clear that health is a part of welfare. Pathology is  
21 the detrimental derangement of molecules, cells and functions that occurs in living  
22 organisms in response to injurious agents or deprivations (Broom and Kirkden 2004,

1 modified after Jones et al 1997 who omit the word “detrimental”)Pathology is also the  
2 study of such conditions. Table 1 shows types of pathology with examples.

3

4 Table 1. Pathology categorised according to causes

5

<u>Causation category</u>	<u>Examples</u>
Genetic abnormalities.	Congenital hip dysplasia in dogs; femoral head necrosis in fast-growing broilers.
Physical thermal and chemical injuries.	Hyperthermia and its consequences.
Infections and infestations	Foot and mouth disease; sheep scab.
Metabolic abnormalities	Hoof disorders in cattle fed too much concentrated food in proportion to roughage.
Nutritional disorders	Over-eating; vitamin deficiencies.

6

(modified after Slauson and Cooper 1990)

7

1 Any kind of pathology involves some degree of poor welfare. If an individual has a  
2 parasite or pathogen within its body, it may be that there is no effect upon that individual  
3 so no pathology or effect on welfare. However, as soon as there is “detrimental  
4 derangement”, as described in the definition of pathology, the individual will have more  
5 difficulty in coping with its environment and some harmful effect on its functioning so  
6 there will be worse welfare because of the pathology. It might be that the individual is  
7 aware of the consequences of infection and the pathology might lead to feelings of pain  
8 or malaise. In that case the pain or malaise plus the other effects of the pathology will  
9 make the welfare worse than when there is pathology alone. Consider a sheep infested  
10 with the sheep scab mite *Psoroptes ovis*. The mite can be present without affecting the  
11 sheep so there is no pathology and no effect on welfare. However, mite activity on the  
12 skin leads to an inflammatory response, lesions, biochemical changes in the blood,  
13 irritation and rubbing responses, changes in blood cell counts and hormones, mouthing  
14 stereotypies, changes in pain sensitivity and often death (Corke 1997, Corke and Broom  
15 1999, Broom and Corke 2002). Welfare can be assessed during changes in the extent of  
16 pathology in sheep with sheep scab (Table 2). Some of the variables mentioned in this  
17 table will always result in some degree of poor welfare whilst others can indicate good or  
18 poor welfare. Animals with pathology, whether from infectious disease, metabolic or  
19 other disorders can have very poor welfare which can be evaluated scientifically.

20

21 Table 2 Welfare and its assessment in sheep with sheep scab

22

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1. Means of assessing welfare:	clinical examination
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	behavioural assessment
	nociceptor response
	physiological assessment
	immune system function

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2. Variables affecting welfare:
- body condition score
  - lesion dimensions
  - mite numbers
  - skin sensitivity
  - body temperature
- 

1 (modified after Broom and Corke 2002)

2

3 In some animal housing and management systems the most important causes of poor  
 4 welfare are disease conditions. For example, the major welfare problems of dairy cows  
 5 are leg disorders and mastitis; reproductive disorders and behaviour restriction are of  
 6 somewhat less importance (Webster 1993, Greenough and Weaver 1996, Broom 1999,  
 7 2001b, Galindo and Broom 2000). In high producing herds there are about 40 cases of  
 8 leg disorders and lameness per 100 cows per annum. These disease conditions will vary  
 9 with the environmental conditions but are also considerably affected by the metabolic  
 10 pressures on the individual. Cows which produce very large quantities of milk are much  
 11 more likely to be overtaxed metabolically and hence to have such problems (Pryce *et al*  
 12 1997).

13

1 Another example, which involves the largest numbers of animals kept by man, is the  
2 broiler chicken. In chickens kept for meat production, the major causes of poor welfare  
3 are pathologies which result from selection for fast growth. Some of the problems that  
4 have arisen in the very fast growing birds are those associated with the cardiovascular  
5 disorders which lead to ascites. A larger proportion of the problems are those leg  
6 disorders which result in reduced ability to walk, for example tibial dyschondroplasia,  
7 femoral head necrosis and valgus-varus syndrome (Broom 2001a, Bradshaw et al 2002),.  
8 Reduced ability to walk or stand often results in breast blisters and hock burn because the  
9 bird has to spend a long time crouching on poor quality litter. In a recent study in  
10 supermarkets, 82% of grade a birds had some degree of hock burn (Broom and Reefman  
11 2005). The dermatitis seen in such birds is painful in itself but the effects of inability to  
12 walk are much more severe.

13 It is quite clear that disease will cause poor welfare. However, poor welfare, resulting  
14 from a wide variety of different causes, may make disease more likely, often by initiating  
15 immuno-suppression (Kelly 1980, Broom 1988, Broom and Kirkden 2004). Depression  
16 can be a consequence of an environment that is difficult, perhaps because the individual  
17 has little control over it, and this condition which certainly involves poor welfare, has  
18 further pathological consequences (Irwin 2001). It is also possible for injurious  
19 behaviour, which is caused to one individual by another and is often associated with poor  
20 welfare in both, to increase the likelihood or extent of pathology. On the other hand,  
21 good welfare, sometimes facilitated by the social support provided by conspecifics, can  
22 help to protect individuals against disease (Sachser 2001, Lutgendorf 2001). Positive  
23 behavioural and mental responses can increase the likelihood that the individual will



1 succeed in coping. Indeed pathologies, such as tumour growth and proliferation, can be  
2 reduced or prevented, in humans and perhaps in other species, by being happy and  
3 thinking positively (Broom and Zanella 2004). Welfare has important and complex inter-  
4 relationships with pathology.

5

#### 6 **4. Adrenal and other coping methods in relation to disease.**

7

8 If, at some particular time, an individual has no problems to deal with, that individual will  
9 be functioning well and will have good brain state and feelings as well as normal body  
10 physiology and behaviour. Another individual may face problems in life that are such  
11 that it is unable to cope with them. Coping implies having control of mental and bodily  
12 stability and prolonged failure to cope results in failure to grow, failure to reproduce or  
13 death (Broom and Johnson 1993). A third individual might face problems but, using its  
14 array of coping mechanisms, be able to cope but only with difficulty. The second and  
15 third individuals are likely to show some direct signs of their potential failure to cope or  
16 difficulty in coping and they are also likely to have had bad feelings associated with their  
17 situations.

18 Pathogens elicit a range of responses in animals, including a set of immunological  
19 responses which include proliferation and activation of: (i) B-cells synthesising  
20 antibodies that bind to antigens thus facilitating antigen ingestion by granulocytes and  
21 macrophages or destruction by complement, which is a set of enzymes; (ii) T-cells which  
22 destroy cells with foreign antigens on their surfaces; (iii) T-helper cells which assist (i)  
23 or (ii); (iv) NK –cells which destroy cells that lack normal antigens, such as tumour cells

1 or those containing viruses; and (v) memory cells which increase humoral and cell-  
2 mediated responses. These and other defence mechanisms against pathology interact  
3 with other coping systems as explained below.

4

5 Glucocorticoids play an important part in many body-regulating functions and facilitate  
6 important adaptive brain processes (Broom and Zanella 2004). However, cortisol or  
7 corticosterone may be produced in emergency situations where coping is difficult. High  
8 levels of cortisol have been shown to: decrease interleukin-1 synthesis by macrophages  
9 and of interleukin-2 by T-helper cells causing poorer B-lymphocyte and cytotoxic T-cell  
10 activity; decrease interleukin-beta that regulates T-helper cell -1 and -2 balance and  
11 action; and result in generally worse effects of respiratory pathogens, Toxoplasma,  
12 Salmonella and tumours (Dantzer 2001, McEwen 2001, Broom and Kirkden 2004).

13

14 Some of the situations which elicit glucocorticoid production have rapid and serious  
15 effects on the health of the animals. In a recent report of clinical cases by Madel (2005) a  
16 group of elderly sheep had been gathered, transported for 30 km and then left on an  
17 exposed field during a stormy night. At least thirteen of the sheep became hypocalcaemic  
18 and three died by the following morning.

19

20 There are many other examples of stress leading to pathology. Adrenal activity can be  
21 followed by arteriosclerosis, myocardial lesions, gastric ulcers and various other forms of  
22 organ damage (Manser 1992).

23

1 As explained in detail by Broom and Kirkden (2004), the relationship between the  
2 chronic activation of physiological coping mechanisms, immunomodulation and  
3 susceptibility to infectious disease has been explored in the field of  
4 psychoneuroimmunology. Environmental challenges which lead to poor welfare, whether  
5 they threaten mental or bodily stability, activate these coping mechanisms. However, the  
6 relationship is not a simple one. The response of the neuroendocrine system varies  
7 according to environmental challenge (Mason 1968a,b, 1975), species (Griffin 1989) and  
8 how individuals perceive the challenge. Glucocorticoids and other hormones modulate  
9 the immune system in various ways but a given change in the immune system may affect  
10 an animal's susceptibility to different pathogens in different ways (Gross & Colmano  
11 1969).

12 Glucocorticoids have been known for some time to have certain effects on the immune  
13 system (Griffin 1989): reduction in the number of circulating lymphocytes  
14 (lymphopaenia); increase in the number of neutrophils (neutrophilia); in many species  
15 reduction in the number of eosinophils (eosinopaenia); a drop in the total number of  
16 circulating leucocytes (leucopaenia); or in species with relatively low numbers of  
17 lymphocytes, an increased leucocyte count (leucocytosis). The differential effects of  
18 glucocorticoids upon different leucocyte populations may explain the observation that a  
19 given stressor can increase the susceptibility of chickens to some pathogens whilst  
20 reducing their susceptibility to others (Gross & Siegel 1965, 1975, Siegel 1980). Not only  
21 do glucocorticoids reduce the number of circulating lymphocytes, they also suppress the  
22 activity of B cells and cytotoxic T cells, by interacting with macrophages and T-helper  
23 cells. For example, glucocorticoids decrease the synthesis of interleukin 1 (IL-1) by

1 macrophages (MacDermott & Stacey 1981) and the synthesis of interleukin 2 (IL-2) by  
2 T-helper cells (Gillis et al. 1979). These cytokines increase the activity of B cells and  
3 cytotoxic T cells, as well as that of other leucocytes, including macrophages and T-helper  
4 cells.

5 Glucocorticoids are very important mediators of the immune system but they are not the  
6 only means by which stressors influence immunocompetence (Griffin 1989; Biondi &  
7 Zannino 1997; Yang & Glaser 2000). Other hormones produced when animals are trying  
8 to cope with difficulties in life include beta-endorphin, vasopressin and oxytocin. It is  
9 known that beta-endorphin can promote T-cell responses and that vasopressin and  
10 oxytocin stimulate T-helper cells to produce interferon-gamma which, in this  
11 circumstance, activates NK cells and macrophages. Oxytocin is produced during  
12 mammalian nursing of young and various other pleasant experiences (Carter 2001).  
13 Hence it seems that pleasure can sometimes lead to better defence against pathogens  
14 (Panksepp 1998).

15 Both the synthesis of  $\beta$ -endorphin by the anterior pituitary gland (Haynes & Timms  
16 1987) and the release of vasopressin and oxytocin from the neurohypophysis (Wideman  
17 & Murphy 1985; Williams et al. 1985) are increased in response to environmental  
18 challenges. In humans at least, catecholamines suppress the cell-mediated immune  
19 response whilst enhancing the humoral immune response (Yang & Glaser 2000).  
20 Furthermore, the lymphoid organs, including the bone marrow, thymus, spleen and lymph  
21 nodes, where lymphocytes are produced and stored, are all innervated (Felten & Felten  
22 1991; Schorr & Arnason 1999), permitting the CNS to influence lymphocytes directly.  
23 Vasopressin and oxytocin (Gibbs 1986a,b; Gaillard & Al-Damluji 1987) and

1 catecholamines (Axelrod 1984) also stimulate the secretion of ACTH, whilst  $\beta$ -endorphin  
2 is secreted in parallel with ACTH, from their mutual precursor pro-opiomelanocortin  
3 (Guillemin et al. 1977; Rossier et al. 1977).

4 Environmental conditions which elicit physiological coping responses in animals, thus  
5 involving poor welfare, alter their susceptibility to infectious agents and hence their  
6 health (Peterson et al. 1991; Biondi & Zannino 1997).

7

8

9

10 The wide range of responses to pathology includes behavioural changes, physiological  
11 changes in the body such as the production of acute-phase proteins in body fluids and  
12 production of cytokines in the brain as well as immunological changes. Short-term  
13 responses to pathological effects include vomiting, which gets rid of some toxins and is  
14 promoted by certain interferons, and diarrhoea which also helps to get rid of toxins and is  
15 promoted by interleukin-2. Longer-term responses include malaise or sickness behaviour  
16 which is linked to immunological changes (Hart 1988, 1990). Immune system responses  
17 may need much energy whilst pathogens may take energy directly from their host. Hence  
18 some sickness behaviour results in energy saving, some promotes body defence  
19 mechanisms, and all is adaptive (Broom 2006). Sickness behaviour is initiated when  
20 cytokines are released by infected cells, endothelial cells, phagocytes, fibroblasts and  
21 lymphocytes so there are many peripheral sources as well as brain-mediated sources  
22 (Gregory 1998, 2004). However, the importance of the brain in relation to responses to  
23 pathogens is clear from brain lesion studies. Lesions to the hypothalamus and reticular

1 formation reduce cellular immune responses whilst lesions to the locus coeruleus reduce  
2 antibody responses (McEwan 2001).

3

#### 4 **5. Some adaptive cytokine responses to pathology**

5

6 At the individual level, adaptation is the use of regulatory systems, with their behavioural  
7 and physiological components, to help an individual to cope with its environmental  
8 conditions (Broom 2006). Welfare may be good or poor while adaptation is occurring.  
9 Some adaptation is very easy and energetically cheap so, during this, welfare can be very  
10 good. Other adaptation is difficult and may involve emergency physiological responses  
11 or abnormal behaviour, often with bad feelings such as pain or fear. In that case, welfare  
12 is poor or very poor even if complete adaptation eventually occurs and there is no long-  
13 term threat to the life of the individual. In some circumstances, adaptation may be  
14 unsuccessful, the individual is not able to cope, stress occurs and welfare is ultimately  
15 very poor. One important part of trying to adapt to, or cope with, pathology is the acute  
16 phase response (Kuchner 1988, Gregory 1998). This is a set of body defences initiated  
17 and largely controlled by chemical mediators: the cytokines. Cytokines can affect  
18 leucocyte adhesion, alter capillary permeability, stimulate production of neutrophils,  
19 break down muscle proteins to allow production of acute phase proteins and initiate  
20 fever. Fever is an effect promoted by the cytokines interleukin-1 and interleukin-6.  
21 Fever helps recovery, for example from *Pasteurella multocida* infection, and helps the  
22 infected individual to combat pathogens such as *Babesia* (Hart 1988, Gregory 1998).

1 There is an energetic cost associated with fever but in many cases the response is life-  
2 saving.

3  
4 A quite different adaptive effect of cytokines in sick animals is to cause loss of appetite.  
5 This saves energy in the short-term because gut activity does not occur. Fasting has been  
6 shown to reduce the *Listeria* population in the body of mice and to reduce mortality rates  
7 (Wing and Young 1980). Failure to eat with consequent reduction in energy availability  
8 can, however, harm immunological defences if prolonged (Dallman 2001). Brain  
9 processing efficiency can be impaired by some cytokine activity, perhaps because of  
10 reduction in energy availability.

11  
12 A wide range of other effects are caused by cytokines in response to pathology (Table 3).  
13 Wound-healing is promoted by TGF-beta-2 and the anti-inflammatory cytokines  
14 interleukin-4, interleukin-10 and TGF-beta help to control septic shock caused by internal  
15 poisons which might be produced by pathogen action.

16  
17 Table 3. Sources and actions of three cytokines, interleukin-1(IL-1) interleukin-6(IL-6)  
18 and tumour necrosis factor(TNF) that initiate sickness behaviour

<u>Cytokine</u>	<u>Source</u>	<u>Principal Actions</u>	<u>CNS Effects</u>
IL-1	Macrophages	Circulating neutrophils	Fever
	Fibroblasts	Colony stimulating factors secreted	Sleep
	Endothelial cells	Capillary permeability	CRF* secretion

	Monocytes	Prostaglandin synthesis	Inappetance
		Leucocyte adhesion	Memory
		Endothelial adhesion	impairment
IL-6	Fibroblasts	Immunoglobulin synthesis	Fever
	Tumour cells	and secretion in B-lymphocytes	
	Macrophages		
	Endothelial cells		
TNF	Macrophages	Haemorrhagic necrosis in tumours	Fever
	Monocytes	Lysis of bone	
	T-lymphocytes	Leucocyte adhesion	
		Endothelial adhesion	
		Granulomas induced	
		Blood coagulation aided	

1 \* CRF – corticotrophin releasing factor/hormone (modified after Gregory 1998)

2

3 The most dramatic sickness behaviour when animals have some degree of pathology is  
4 often reduced activity (Gregory 1998, 2004). The individual may feel tired, rest and sleep  
5 more. This is adaptive because sleep deprivation and too much activity when fatigued  
6 can lead to a reduction in natural killer (NK) cell activity and a reduction in interleukin-2  
7 response to antigen challenge (Irwin et al 1994). It is also known that interleukin-



1    1increase leads to more non-REM (rapid eye movement) sleep. A second kind of  
2    reduced activity is that caused by pain. This is promoted by interleukin-2. The feeling of  
3    pain itself can be mediated via products of damaged tissue, such as nitric oxide, which  
4    promote the action of inflammatory agents such as bradykinin and prostanoids (Dray et al  
5    1995).

6

7    A third type of activity reduction is that which results when the individual socially  
8    isolates itself. This will be adaptive because an isolated, infected individual whose  
9    activity is reduced is less likely to transmit infection or have other infections transmitted  
10   to it. All three kinds of activity reduction can help an individual to recover from disease.

11

## 12    **Conclusions**

13

14   Behaviour plays an important part in disease transmission and in medical and veterinary  
15   diagnosis of disease, whilst disease has had effects on the evolution of behaviour. The  
16   health of an animal is its state as regards its attempts to cope with pathology and  
17   pathology is the detrimental derangement of molecules, cells and functions that occurs in  
18   living organisms in response to injurious agents or deprivations. Hence, health is an  
19   important part of welfare and pathology is both a cause of poor welfare and is affected by  
20   poor welfare. It is important to develop better quantitative methods for measuring the  
21   welfare of diseased animals. Disease transmission, and as a consequence important  
22   aspects of animal welfare, farm animal economics and human welfare, can be understood  
23   better if knowledge of animal behaviour and brain function are utilised. On the other

1 hand, the approaches used in research on diseases, including epidemiology (Rushen  
2 2003), can be of value in animal welfare research. Similarly, understanding of some  
3 behaviour requires a knowledge of disease and bodily responses to it. There is a need for  
4 interdisciplinary co-operation in order that these areas of science can be further  
5 developed.

6

### 7 **Acknowledgements**

8

9 I thank Gareth Pearce, Murray Corke, Neville Gregory and journal reviewers and editors  
10 for helpful discussions and comments.

11

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