THE DALMATIAN DILEMMA

White Coat Colour and Deafness.

by
DR. BRUCE M CATTANACH
MRC Mammalian Genetics Unit, Harwell,
Oxfordshire OX11 0JJ, UK

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The Dalmatian, despite the presence of its pigmented spots, is basically a white dog and, as a breed, is widely reported to have a notably high risk of deafness (Table 1).

Although the association of deafness with white coat colour has long been recognised, veterinary researchers have been perplexed by the inheritance of the deafness component. Thus, it has evident to all that hearing dogs when mated together can produce deaf pups, but it has also been found that deaf dogs mated together can produce hearing pups.

Variable sex differences in incidence of deafness have also been reported. As a consequence recessive, dominant, multi-factorial and even sex-linked inheritances have been postulated (see Greibrokk 1994; Anderson *et al* 1968).

Despite this confusion it has been shown in studies conducted both in the UK and America that selective breeding for hearing dogs can reduce the incidence of deafness.

This has been greatly facilitated by "BAER testing" (brain stem auditory-evoked response) which allows unilaterally affected dogs (deaf in only one ear) to be distinguished from totally normal animals.

There is therefore the potential for breeders to reduce the incidence of deafness in their stocks.

Molecular genetic approaches to identify genes for deafness have also been contemplated in the hope that this might further assist breeders in selecting dogs that are free of deafness genes.

This report is written on behalf of the KC/BSAVA sub-committee to present a less complex genetic basis for the deafness in white dogs; it represents a geneticist's interpretation of the published findings made both in dogs and laboratory mice.

Perhaps surprisingly, the basis of the deafness is not recognised in terms of deafness genes, but rather upon the recognised mechanisms by which pigmented and unpigmented (white) areas are produced throughout the body, be they in the coat or elsewhere.

Unfortunately the implications create something of a dilemma for Dalmatian breeders. As already implied by Famula *et al* (1996) and Wood *et al* (1996), they suggest that positive selection for hearing dogs will be offset by negative selection to meet the demands of the Breed Standard.

The basis of white coat colour

The white coat colour of dogs can be brought about by one or other of two ways. It may result from an extreme dilution of the pigment produced by pigment cells such that some degree of off-white shading may be evident. A breed showing this form of white coat is the West Highland White Terrier which may often show a "shading" on the ears or along the back.

The second form of white coat colour results from the actual absence of pigment cells. This form of white coat is found in breeds in which distinct patches of fully pigmented coat are occasionally or commonly found. These commonly occur around the eyes and ears but such distinct patches may also be found on the body. The white areas or markings on dogs which are predominantly pigmented can also be attributed to this cause.

At least two genes are known to cause white areas by the absence or diminution in numbers of pigment cells.

One is the dominant merle (*M*) gene, commonly carried in the heterozygous (single dose) form in breeds of Collies, as well as Cardigan Corgis and Harlequin Great Danes. It is the homozygote with two doses of the gene that is principally affected, typically being totally white. Because the homozygote is also liable to be blind and deaf as well as being otherwise severely impaired, matings that would produce such dogs are usually avoided.

A second gene that reduces the numbers of pigment cells to cause a white coat colour is the recessive (*s*) gene, the extreme allele or form of which gives the near all white coat typically seen in Dalmatians, English Setters, white Bull Terriers, white Boxers, etc.

There are several different alleles of the *s* gene, these bringing about characteristically different levels and distributions of white coat.

The top dominant allele, *S* or +, gives the essentially solid coloured coat seen in many breeds, but minor levels of white may be found on the toes, chest and belly.

The next allele is that for the so-called Irish spotting (s^i). Here, the white markings are principally located on the foreface, around the neck, on the lower limbs, chest and belly. Breeds carrying this allele are the Boston Terrier and Basenji.

Then there is the piebald spotting allele (s^p) which has a wider distribution of white as illustrated in some Cocker Spaniels and Pointers.

And, finally, there is the extreme white spotting allele (s^w) found in Dalmatians and other breeds previously mentioned (Table 1). In these dogs, almost the entire coat is white (ignoring the pigmented spots for the moment) but pigmented patches, as previously described, can sometimes also be found. Elucidation of these pigmented/non-pigmented patterns provides an important clue for the relationship between white coat colour and deafness.

Studies in laboratory mice have shown that the pigment cells derive from the neural crest of the foetus. Prior to birth, they migrate from this tissue and colonize pairs of specific sites on each side of the head and the backline of the body. Three pairs of sites exist on the head. One site lies close to the eye, another lies close to the ear, and a third lies at the occiput, the latter no doubt being the basis of the Blenheim spot of Cavaliers King Charles Spaniels.

Various estimates suggest that there are about six sites along each side of the body, with a possible larger number along the tail (Schaible 1969; Mintz and Russell 1967; Cattanach 1974). At each site one or a very few pigment cells (maybe up to three, Lyon 1970) proliferate to give clones of cells which migrate outwards so that they join up, but they also spread down each side of the head and body until they meet up on the underside, and further spread down the legs towards the toes. The most remote regions (under the chin, chest, belly and lower limbs) are the most at risk of remaining uncolonised by the pigment cells and therefore white. This is the most common basis of the white markings seen in many species, dogs, cats, mice, horses, cattle etc.

The various *s* alleles both reduce the number of pigment cells and impair their migration to different degrees. With the normal *S* allele, full pigmentation typically occurs, but the most remote areas (notably chest and toes) are most at risk of being uncolonised. Hence the occasional white markings on the chest, belly and toes of solid breeds such as the Irish Setter.

With the s^i allele, the initiating sites on the neck may never gain their single pigment cells and elsewhere pigment cell migration is generally impaired. Hence the white collar and extensive white markings in such animals.

The same mechanism may apply more widely with s^p to give the piebald pattern, and with the extreme s^w, most of the coat is white with only the occasional pigmented patch seen in regions close to the original sites, notably those around the eyes and ears. In all cases the boundaries represent the "tide marks" of the pigment cell migration. In dogs, this spread clearly continues after birth, patch size increasing and white areas decreasing over the first few days or weeks.

While the spread or migration of the pigment cells produces the characteristic patterns that are so familiar in dogs, this is not the whole story. This is best illustrated by the regular occurrence of pigmented spots on the skin of white regions, with the hair in these spots occasionally also being affected. It is likely that the ticking (*T*) factor of Dalmatians only exaggerates this normal phenomenon to give the spotted pattern that characterises the breed. There has been much scientific controversy over the mechanisms responsible but it seems likely that pigment cell migration initially covers the whole of the body. There is then a period (before birth) in which most pigment cells in the potentially white areas fail to

survive. Then proliferation and migration restarts (after birth) as can readily be observed in dogs to give the final "tide mark" patterns seen in s^i and s^p animals and the appearance in Dalmatians of spots within the white areas where single pigment cells have survived. However, while such theory may be important for the genetics of spotting/ticking it probably has little relevance for the issue of deafness.

It should be noted that there is a considerable variation in the amount of white coat shown by dogs possessing the various *s* alleles, and in both dogs (Robinson 1982) and laboratory mice (Schaible 1969; Gruneberg 1952) it has been found that the levels can be readily modified by selective breeding. Thus, starting from an intermediate level of white, selection upwards can generate near-all white animals and selection downwards can produce near-solid ones. There can also be considerable right-left asymmetry. For example, there may be a pigmented patch around an eye or ear on one side of the head but not on the other. Beyond this, with greater amounts of white, one or both eyes may be completely or partially blue, this resulting from the absence or near-absence of pigmentation within the iris.

Overall, therefore, there is a significant chance element to the pigment cell distribution. This is important as pigment cells also colonize the inner ear and play an as yet undefined but essential role in maintaining its function.

The basis of deafness

Apart from external factors, many different genes are known to cause deafness in both laboratory mice (Steel 1995) and dogs (Strain 1996), this attributable to specific types of abnormalities within the inner ear.

The type associated with white coat colour is described as sensorineuronal. It has been shown in mice that the presence of pigment cells is essential for normal inner ear development. They normally colonize the stria vascularis. However, in their absence, as is also well documented in the dog, the stria vascularis degenerates. As this provides the blood supply to the cochlea, damage to this structure occurs and the sensory hair cells necessary for hearing die.

Clearly the effect is variable as BAER testing has demonstrated that one, both, or neither ear may be affected.

Pigment cells are invariably absent from the stria of deaf mice which have a white coat colour attributable to pigment cell deficiency.

The relationship of deafness with white coat colour and blue eyes is therefore clear. In all cases the lack of pigment cells is responsible. The fewer the number and the more limited pigment cell spread, the greater the proportion of the coat lacking these cells and appearing white. Similarly, there is also the greater the risk of one or both eyes being unpigmented to give the blue appearance. And, most importantly for this report, there is also the greater risk of pigment cells being absent from the stria of one or both ears to result in unilateral or bilateral deafness.

On the basis of these findings there is no need to postulate specific single or multiple genes for deafness or blue eyes in pigment cell deficient white dogs. All the effects are attributable to the *s* gene.

The incidence of deafness in Dalmatians

Table 2 presents some of the estimates of deafness in Dalmatians. While there was some indication of a region by region variation within America and also national variations, the data overall are remarkably consistent.

At all locations, the incidences were high, and the problem has not been not restricted to particular lines or sections of the breed. This in itself speaks against a gene for deafness being involved. Moreover, the BAER testing results showed that the estimates of bilaterally deaf dogs minimise the problem.

The frequency of unilaterally affected animals in all regions was generally two to three times higher than that of totally deaf animals. A very high proportion of the breed (20 - 30%) therefore suffers some level of the defect.

The association of blue eyes with deafness
The association of blue eyes with deafness in white dogs has been recognised since the first reported case in 1896(Rawitz, in Hayes 1981).

Some of the recent key evidence is summarised in Table 3.

It may be seen that the risks of both bilateral and unilateral deafness in blue eyed dogs are about 2 - 3 times higher than in brown eyed dogs, and even the presence of one blue eye signals almost the same high level of risk.

Greibrokk (1994) has attributed to the relatively low incidence of deafness in Norwegian Dalmatians (Table 2.) to breeder selection against blue eyes. This may also be true for British Dalmatians which also show a lower incidence of deafness (Wood and Lakhani 1997) than their counterparts in America where blue eyes are reportedly (Greibrokk 1994) tolerated for show purposes.
The link of blue eyes with deafness is also suggested in Strain *et al*'s (1992) report of a single American Dalmatian dog which was thought to be "free of a gene for deafness" on the basis of that he produced only 13 (6.2%) unilaterally deaf and 2 (1%) bilaterally deaf puppies among 210 recorded in 25 litters, as compared with 21.8% and 8.0%, respectively, in the study overall (Table 2.).

Significantly, only 2 of the puppies (1%) had blue eyes compared with 10.6% recorded elsewhere in the Strain study. Greibrokk (1994) has also pointed out that a lower incidence of deafness was achieved in Norway by selecting against blue eyes than achieved in America (Strain *et al* 1992) by selecting against unilateral and bilateral deafness.

Selection against blue eyes and hence for eye pigmentation, implies selection for more pigment cells or greater pigment cell spread. It is therefore to be expected that the probability of pigment cells reaching the inner ear will be higher to cause a reduction in the incidence of deafness.

The association of pigmented patches with a reduced risk of deafness

Many investigators have pointed to the reduced incidence of deafness in Dalmatians with pigmented patches (Strain *et al* 1992; Holliday 1992, Greibrokk 1994, Famula *et al* 1996; Strain and Tedford 1996).

The most compelling data are presented in Table 4. Bilateral deafness in patched animals was consistently lower (about 2%) than that found in dogs without patches (about 8.4%). Likewise, the frequency of unilateral deafness was also substantially reduced (8.5% to 23.5%).

The relationship between patching and lower incidence of deafness was also seen among the progeny of the single male described by Strain *et al* (1992) that produced a low incidence of deafness. Among his 210 puppies a high proportion (21.9%) were patched compared with the lower overall frequency (9.8%) in the main study.

Consistent with the association between patching and a reduced incidence of deafness in Dalmatians is the observation that in Bull Terriers, where there appears to be breeder tolerance of head patching, the incidence of deafness is lower than found in Dalmatians (Table 1).

In laboratory mice it has also been noted that the more extreme the amount of white areas in the coat, the greater the likelihood of an absence of pigment cells in the inner ear and the greater the risk of deafness (Steel 1995).

Just as selection against blue eyes has been found to reduce the incidence of deafness, it may be expected that selection for patches would have the same effect.

Test for other factors

Strain (1992) has screened for other factors which might influence the incidence of deafness. These included sex, colour (black, liver, lemon, tricolour),retinal pigmentation, eye rim and nose pigmentation, spot size and level of marking.

Inconsistent results were obtained for several of these characters at the three American test sites tested (Table 2), but only retinal pigmentation (in addition iris pigmentation and presence of patches) showed an association with deafness.

Sex differences have been suggested (Holliday 1992; Wood & Lakhani 1997) but have not been observed in the other studies cited.

Breeding data and deafness

Many investigators have noted that Dalmatians with normal hearing in both ears, as shown by BAER testing, produce fewer affected puppies than those showing evidence of deafness (Strain 1992, 1996; Yuzbasijan-Gurkan 1994, Tedford 1996; Wood and Lakhani 1997).

Some of the key data are presented in Table 5.

In Yuzbasiyan-Gurkan's (1994) study upon American dogs the incidence of bilaterally deaf dogs was three times higher among the progeny from unilaterally affected x normal crosses than from normal x normal crosses.

More detail is provided by Strain and Tedford's (1996) study which shows that both bilaterally and unilaterally deaf puppies to be much more common from affected x normal matings than from normal x normal matings.

A similar result is suggested in Wood and Lakhani's (1997) smaller study upon British Dalmatians.
Such findings provide the evidence that deafness of white dogs, and Dalmatians in particular, has a genetic component.

As has already been mentioned, however, it is well-established that the amount of white coat associated with the *s* gene in both mice (Schaible 1969; Gruneberg 1952) and dogs (Robinson 1982) readily responds to selection.

Since this change in the coat results from a change in the numbers or migration of pigment cells, it would be surprising if this effect did not extend to the inner ear to give a correlated increase or decrease in the incidence of deafness. Such changes in effect simply reflect shifts in expression of the *s* gene brought about by modification of the "genetic background".

There is no need to hypothesise separate genes for white coat colour, blue eyes, and deafness in white dogs. The *s* gene (or *M* gene in other breeds) is the common genetic causal factor.

Implications for the control of deafness
It should be clear from the above that white coat, especially in the absence of pigmented patches, blue eyes and deafness are intrinsically linked. All have the common basis of absence of pigment cells.

It should also be clear from the findings described that each type of effect can be modified by selective breeding.
Both the American and UK Dalmatian data show that deafness can be reduced by selection; it has been shown in Norwegian Dalmatians that blue eyes can similarly be reduced; and it has long been recognised both in laboratory mice and dogs that selection can modify the extent of pigmented areas in the coat which in minor degree are seen as patches.

The response to selection for any one of these characters implies that pigment cell numbers and/or migration is being modified. It follows that selection for any one character will modify the others and this points to the Dalmatian dilemma.

Selection for hearing (whether by BAER testing or DNA approaches), or against blue eyes (Greibrokk 1994), may be expected to increase the incidence of dogs with the pigmented

patches. But, the presence of patches does not accord with the breed Standard. There is therefore breeder selection against patches, and this means unwitting reverse selection for deafness.
To expect that selection against deafness will lead to the production of hearing dogs without patches is asking a lot. It means that in some way it is possible to increase the numbers and/or migration of the pigment cells such that there is an increased chance of them specifically reaching the stria of the inner ear but not regions of the skin and coat.

Amazing things have been achieved in dogs by selective breeding but this would represent the hardest of all. It is rather like expecting to be able to breed s^i or s^p dogs with long white socks on one their forelegs but full pigmenation of the other. Variations between extent of white on the legs does occur but generally the amounts will tend to be similar. To change this by selection must be virtually impossible.

A way forward
I understand that Dalmatian breeders are generally giving a significant support to BAER testing. This, however, records only the one character, hearing. As far as I am aware, no note is made of eye colour or patches.

In view of the association between the three characters it would seem wise to record all the data at the same time and consolidate them in a way that breeders can see for themselves the association. It would not be difficult to produce diagrams that could allow left/right eye colour, and patch size and location to be recorded as well as BAER results on each ear.

The critical question is how to utilise the results to reduce the incidence of deafness in the breed.
Here I would suggest that compromise should be the byword.
There would seem to be no justification at all for breeding from bilaterally deaf dogs and I would imagine that few breeders would disagree with this. But, what about the unilaterally affected dogs? They are outwardly perfectly normal, yet the breeding results show that such partially affected animals are likely have more affected offspring than those with normal hearing (Table 5).

It would therefore be most effective to take all of these dogs out of the breeding population. However, they are too numerous, making up perhaps 20% of the Dalmatian breed. Such stringent selection is too severe to be tolerated.

A compromise solution might be to give some leeway to bitches according to individual breeder needs but treat stud dogs more rigorously. However, anything that would favour the truly normal dogs for breeding could be considered.
The data accumulated further indicate that risks of deafness can be reduced by discarding blue eyed dogs from the breeding population, and I suspect few UK breeders would find any difficulty with this. However, the more controversial issue is the patching.

Selection against patched animals must already be a burden on the breed, as well as enhancing the risks of deafness. Surely there must be scope for compromise.

Were limited patching around the ear or eye made acceptable within the Standard, the incidence of deafness might drop as low as that found in white Bull Terriers (Table 1) and there might be scope for further improvement by selection.

This would virtually eliminate totally deaf animals from the breed, which is the most that Dalmatian breeders can realistically hope for and all that is essentially needed.

Table 1.
Breed specific deafness attributable to *s* and *M* alleles

breed	bilaterally deaf	Unilaterally deaf	normal	total	genotype
American Dalmatians	8.0%	.8%	.2%	66*	s^w
White Bull Terrier	1.5%	.5%	.0%	9	s^w
English Setter	2.4%	.7%	.9%	0	s^w
English Cocker Spanial	1.8%	.0%	.2%	8	s^p
Coloured Bull Terrier	0.0%	.1%	.9%	2	s^w?
Australian Cattle Dog	2.9%	.5%	.6%	0	+
Norwegian Dunkerhound	75.0%		.0%	?	*M*

- from Strain *et al* (1992), Strain (1996) and Strain and Tedford (1996)

Table 2
Incidences of deafness in Dalmatians

:searchers	bilaterally deaf	unilaterally deaf	normal	# of dogs
:ain *et al*, USA (1992)				
LA group	12.7%	22.5%	64.7%	377
AZ group	5.9%	23.3%	70.8%	305
CA group	4.9%	19.2%	75.9%	349
Strain, USA (1996)	8.0%	21.8%	70.2%	5379*
Holliday *et al*, USA (1992)	7.0%	21.0%	72.0%	900
Greibrokk, Norway (1994)	4.9%	85.1%+		1843
Famula *et al*, USA (1996)	26.0%**		4.0%	825
Wood & Lakhani, UK (1997)	.3%	13.1%	81.6%	1234

LA = Louisiana; AZ = Arizona; CA = California
* 151 overlap with Holliday group
** Not distinguished
+ not BAER tested

Table 3
Association of blue eyes with deafness in Dalmatians

Researchers	eye colour	bilaterally deaf	unilaterally deaf	normal	# of dogs
Strain *et al* (1992)	brown/Brown	.9%	.3%	.8%	915
	brown/Blue	.4%	.3%	.3%	76

	blue/Blue	.5%	.8%	.8%	32
Holliday *et*	brown/Brown	.6%	.8%	.5%	799
(1992)	brown/Blue	.8%	.5%	.7%	76
	blue/Blue	.2%	.3%	.4%	27

Table 4
Association of patches with hearing in Dalmatians

Researchers	Patch	Bilaterally deaf	Unilaterally deaf	Normal	Number of dogs
Strain *et al* (1992)	Present	2.0%	9.2%	88.8%	98
	Absent	8.2%	23.1%	68.8%	906
Strain & Tedford (1996)*	Present	2.0%	8.5%	79.5%	4596
	Absent	8.4%	23.3%	68.3%	

* May include data of Strain *et al* (1992)

Table 5
Selective breeding in Dalmatians

Reference	Parents	Progeny Bilaterally deaf	Unilaterally deaf	Total affected	Normal	Number tested
Yuzbasiyan-Gurkan (1994)	Normal x Normal	3.9%	15.8%	>19.7%+	<80.3%+	>800
	Unilat x Normal	13.3%	14.2%	>27.5%+	<72.5%+	
Strain & Tedford (1996)	Normal x Normal	5.9%	21.3%	27.2%	72.8%	4596
	Affected x Affected*	11.3%	30.3%	41.6%	58.4%	
Wood & Lakhani (1997)	Normal x Normal	4.1%	11.3%	15.4%	84.5%	458
	Unilat x Normal	2.3%	18.6%	20.9%	79.1%	43

* Affected = bilaterally or unilaterally deaf
+ not BAER tested