WHITE HEIFER DISEASE IN A HERD OF DAIRY SHORTHORNS

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The condition known as white heifer disease, although commonest in white heifers of the Shorthorn breed, has been found in roan and more rarely in red Shorthorns, and also in coloured animals of other breeds. The condition appears to be due to failure of development of the Mullerian ducts. It has been referred to as 'imperforate hymen', but this description is apparently not correct. The vagina is frequently shorter than normal, and when the uterus is completely occluded accumulation of fluid behind the constriction gives rise to discomfort and straining. In mild cases the uterus can be stretched surgically, and when this treatment is successful, fertility is restored. A description of the disease and photographs of some specimens, together with a review of the literature, are published in a paper by Spriggs (1946). The cases discussed here were all bred in a large herd of Shorthorns. They were not seen by the author, but were diagnosed by the attendant veterinary surgeon whose findings were kindly put at the disposal of the author by the owner of the herd. The purpose of this paper is to record those facts which have a bearing on the inheritance of the disease.

The material consists of the daughters of 7 bulls, together with some isolated cases, on which there are not full details, sired by a further 3 bulls. The daughters of these bulls, classified by colour and as affected or normal, are set out in Table 1.

The 7 bulls tested sired 9 affected white heifers out of 23, 4 affected roans out of 115, and 1 affected red out of 94. It is clear that the condition is associated with the 'white' gene. It is always possible that some cases classified as white heifer disease may have been some other genital abnormality very similar to, but with a different origin from, white heifer disease. Unless the anatomy, aetiology and genetics of such diseases can be followed in great detail, such errors are always possible. In this case the picture presented is a consistent one, the frequency of abnormalities decreasing rapidly as the number of 'white' genes decrease—being one in a hundred in the homozygous red, one in twenty-five in the heterozygote, and one in two and a half in the homozygous white—which agrees with previous reports.

If we accept the obvious conclusion that the white gene renders heifers carrying it peculiarly susceptible to the disease, we then have to consider why some white heifers are affected and others not. A survey of the herd book shows us that the average incidence of the disease is less than the figure of 1 in 2·6 white heifers found in this herd. Table 2 sets out the results of the survey, which show that the frequency of white females amongst parents is only slightly less than that amongst offspring, which would not be so if some 40% of white females were sterile. Two samples are included, in one of which all offspring are twins (this sample was collected for a different purpose by Dr Robertson, who kindly let me use it). The other is a sample of all births. In the left-hand side of the table the colours of the offspring are listed, in the middle and on the right are the colours of the parents. The frequency of the 'white' gene, **r**, in the two groups suggests that

by the time of registration some selection against white has already taken place. The frequency in the parents is 0·327, and in the offspring 0·314. Assuming random mating amongst the parents, a mortality amongst white heifers of about 20 % before registration would account for the deficiency. A direct check on this point is provided by the outcome of matings of roans with roans. These should result in 1 red to 2 roans to 1 white. In the sample collected here the frequencies were as set out in Table 3. About 32 % of white animals must be supposed to be eliminated at some stage between conception and registration to account for the numbers found. Returning to Table 2, we can calculate from the frequency of genes in the parents that, on the assumption of random mating, 0·107 of the offspring should be white, 0·440 roan and 0·453 red. If the

Table 1

		Female offspring					
		Red		Roan		White	
Bull	Colour	Normal	Affected	Normal	Affected	Normal	Affected
1	Red	18	0	15	1	0	0
2	Roan	17	0	16	0	6	5
3	Roan	27	0	31	0	4	0
4	Roan	16	0	16	1	3	3
5	White	0	0	25	1	0	1
6	Red	7	1	6	0	0	0
7	Roan	9	0	6	1	1	0
3 others		—	—	—	(1)	—	(2)
		94	1	115	4 (1)	14	9 (2)

Table 2

	Calves registered			Parents: Males			Parents: Females		
	Red	Roan	White	Red	Roan	White	Red	Roan	White
Twins	597	590	107	290	324	33	263	328	56
Singles	637	625	125	539	779	69	561	721	105
Total	1234	1215	232	829	1103	102	824	1049	161
Frequency	0·460	0·454	0·087	0·417	0·532	0·050	0·405	0·514	0·081
Frequency of **R**		0·686				0·673			
Frequency of **r**		0·314				0·327			

Table 3

	Mating of roan × roan			
Offspring ...	Red	Roan	White	Total
Found	212	411	138	761
Expected	190·25	380·5	190·25	

whites are reduced to 0·087 by mortality, the frequency of roans would become 0·449 and that of reds 0·462. This is closely in agreement with the frequencies found. In fact we know that mating is not entirely random, for example there is a tendency for white bulls to be mated to red cows, as will be seen from Table 1, in which the white bull is recorded as having only 1 white offspring out of 27, which would easily account for the excess roans.*

* The matings which resulted in the sample of 'singles' recorded here had a small excess of red × white matings, an excess of roan × roan and a deficiency of red × red. According to the frequency of matings—and assuming no disturbing influences—the offspring would be expected with a frequency of 0·433 red, 0·459 roan and 0·108 white. In order to bring the frequency of red up to that found it is necessary to suppose not only elimination of white but also elimination of roan. The picture is complicated, however, by the misclassification of parents and offspring which will have taken place (see Wright, 1917).

We can conclude that mating is nearly random and that mortality amongst white heifers between conception and registration is responsible for the low frequency of '**r**' in offspring of pedigree Shorthorns. Mortality as used here includes failure to register, but as there is economic incentive for registering it is unlikely to be omitted.

If we now turn to the fertility of those whites which reach registration, we can consider to what extent white heifers are eliminated for all causes between registration and calving. Table 2 shows that 0·087 % of registrations are white and that 0·081 % of female parents are white. This is a comparatively small difference and is, in fact, less than the difference between reds registered and the number of female parents that are red. Selection against white bulls, on the other hand, is strong. It would appear from Table 2 that roan females are favoured above both red and white heifers, and that there is little evidence of infertility amongst white females. An inquiry amongst breeders elicited information on the breeding performance of 43 white heifers of which 4, or about 10 %, proved sterile. Another approach, which does not distinguish between infertility and unpopularity, is to search the herd book for offspring of white animals registered, and compare the proportion of white heifers with registered offspring to the proportion of other colours having registered offspring.

Table 4

	No. of potential parents of each colour	No. for which offspring were registered		
		Red	Roan	White
1	28	20	23	19
2	400	156	162	137
Total	428	176	185	156

A sample of white females was taken from the herd book and the red and roan females registered nearest to each white female were used as a control. The herd books 3, 4 and 5 years after the one in which the females were registered were then searched for offspring. In Table 4 the results of this investigation, which was carried out on 28 individuals of each colour, and the result of one carried out on 400, are recorded. In the larger investigation only one herd book—the one 3 years after the samples were registered—was searched for offspring. There is clear evidence that white animals are either less fertile than the others, or are sold more frequently between registration and calving. Compared to red animals their breeding success is down by some 13 %. Taking all lines of evidence together, it appears that white heifers in the population as a whole have a breeding efficiency of 90 % compared to red and that the preference shown for roans is sufficient to maintain the **r** gene in the population.

The question to be answered, then, is why the herd under consideration should be so much more seriously affected by white heifer disease than the general population of Shorthorns. The fact that there are 8 sires for the 17 affected animals argues against the possibility that there is any further genetic factor at work besides the white gene. The only relationship between the 8 bulls is that the sire of one of them was the grandsire of another. They all come from well-known pedigree herds. These form a close-knit population in which, apart from this farm, there is apparently no undue incidence of the disease. Five of the affected white heifers, however, were sired by 1 bull, who was grandsire to a further 5. This is not as indicative as it sounds; 11 of the 25 white heifers listed here were sired by the bull in question, no. 2, and it is not surprising, therefore, that he should have sired 5 out of 11 of the affected white animals. Further, the worst period for the occurrence of the disease

was a 3-year period, 1943–5. The 6 white heifers sired by bull no. 2 before this date were all normal, whereas of the 11 white animals born to all bulls between 1943 and 1945, 9 were affected. This suggests that conditions were peculiarly favourable to the appearance of the disease during these years. A further piece of evidence bearing on the possible genetic basis of the difference between affected and normal white heifers is as follows: all white cows having calves must themselves be more free of auxiliary genetic factors tending to enhance the effect of **r** than the general run of the population, since they have a genotype which enables them to calve normally despite the fact that they are white. Any white daughters they have may be expected to be more fertile than white daughters of roans. The 22 white animals for which the information is available are distributed according to Table 5. The chance of getting this distribution, or one more extreme, calculated according to the exact method described by Fisher (1925), is about 1 in 45. There is thus evidence that, far from having a better chance of being fertile, a white daughter of a white dam has a greater chance of being sterile than a white daughter of a roan dam. In the population in general no supporting evidence could be found for this; 10 out of 24 white heifers, themselves the daughters of whites, were found to have offspring, as against 41 out of 112 whites, the daughters of roans.

Table 5

Colour of dams	White heifers		Total
	Normal	Affected	
White	2	6	8
Roan	11	3	14
	13	9	22

The evidence reported here on the causes of white heifer disease is not conclusive. It is clear, as has been believed for some time and as the name implies, that the chance of a heifer having the disease is increased very considerably by the presence of the white gene, particularly in homozygous condition. Even in heterozygous condition the gene makes an appreciable difference to an animal's chance of being affected. The possibility that modifying genes are responsible for the vagaries of the incidence of affected animals within the **Rr** and **rr** genotypes cannot be ruled out, but it seems somewhat more likely that a combination of environmental factors is at work. If failure of development of the Mullerian ducts is to lead to sterility the trouble may well start during foetal life before fusion of the ducts. This being so, the maternal uterine environment will be an important factor as is strongly suggested by the different incidence amongst white daughters of white and roan dams. If we suppose that the metabolism of white animals is deficient in a way which causes them to be low in the supply of some metabolite necessary for the proper differentiation of the female genitalia, then it follows that white calves who spend their embryonic life in the uterus of white mothers will have the effects of their own defective metabolism reinforced by that of their mothers. We may further suppose that it is at least possible that dietary constituents may influence the occurrence of affected animals, by analogy with the infertility found by Bennetts (1944) and Schinckel (1948) in sheep which have been grazing on subterranean clovers. The infertility was of a quite different type, but the fact that it was undoubtedly brought about by diet makes the suggestion that something of the kind might be responsible for a high incidence of white heifer disease at least tenable.

The effect of the white gene is highly disadvantageous in other respects. We find, in

agreement with Wright, that roan × roan matings give rise to offspring in which white animals are about 30 % too few. As already suggested, the **r** gene is probably maintained in the population because, although roans do not survive to registration any more successfully than reds, they do have more calves. It was shown that whereas 0·460 of the population registered are red and 0·454 roan, only 0·417 of the male parents are red but 0·532 roan, and only 0·405 of the female parents are red but 0·514 of them are roan. The average age of female roan parents was found to be 5·26 years and the age of red and white 5·24 years, so that the increase in frequency of roan parents over roans born is not due to a longer average life after first calving. Since bulls are even more strongly favoured than cows the most likely explanation is that roans are preferred by the farmer. Why they should be preferred is not clear. We have seen that up to registration they have no advantage over reds, and they do not live longer than reds. Records of first lactations, corrected to 305 days, for 257 red, 272 roan and 37 white animals in the same herds expressed as a difference from the herd mean, which was on the average 650 gallons, had the following yields: red, +17·9 gal. ±8; roan, −14·1 gal. ±8; white, −21·8 gal. ±21. There were too few whites to say whether they really do yield less milk than roans or not. There is no doubt that reds are higher yielders than both roan and white. The standard error of the difference of 32 gal. between red and roan is 11 gal. The gene **r** in addition to causing sterility in both heterozygotes and homozygotes and a high calf mortality in homozygotes appears to be a gene for milk yield, the homozygous **RR** having the highest yield, the homozygous **rr** the lowest and the **Rr** an intermediate yield about 5 % below the homozygous **RR**. Since there is an obvious disadvantage in having both white and roan animals in a dairy herd and no obvious counterbalancing advantage, it is difficult to understand why whites should have survived in the breed so long.

In discussing the association of colour with white heifer disease Spriggs refers to the deafness of white bull terriers, and male sterility in a stud of albino horses described by Wriedt (1924), which was confined to the homozygotes. Attention might also be drawn to deafness in white cats and the lightening of hair colour associated with some inherited pathological conditions in man, e.g. phenylketonuria (Penrose, 1949). Perhaps the most interesting comparison is with dominant white spotting in mice (Grüneberg, 1943 and references; Russell & Russell, 1949). One allele, **W**, is lethal when homozygous, but some young live long enough to show that they are black-eyed whites. A second allele is not lethal and in this case homozygous females are usually sterile. The particular interest attaching to this gene from the point of view of white heifer disease is that the heterozygous mouse is in fact a roan. An anaemia is also associated with the gene which may account for lethality and inviability of homozygotes.

SUMMARY

The incidence of white heifer disease in a herd of Shorthorns is described. The disease is far commoner in white animals and somewhat commoner in roan than in red. White animals that were daughters of white seem to be more susceptible than white that are the daughters of roan. From the comparison of the frequency of the gene **r** in registered heifer calves with that in their parents, it was concluded that up to registration there was selection against **r**. This could be accounted for by the inviability or lack of registration of white calves apparent from the deficiency of whites in the offspring of roan by roan matings. After registration, roan animals are favoured by breeders. For this latter preference, no basis could be found either in milk production or longevity.

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