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SHORT PAPERS

The microscopic appearance of waved-2 mouse hairs

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SUMMARY

Hairs from two stocks of homozygous waved-2 mice have been examined. The observations do not agree with a previous report, that the waving was due to a decrease in the proportion of guard hairs and an increase in the number of constrictions per hair, but are consistent with the view that it arises from a defect of keratinization.

The waved-2 (*wa-2*) mutant was first reported by Keeler (1935). The microscopic appearance of the hairs has been described by Reed (1938). I recently examined a series of hair samples from waved-2 mice, and found that my observations failed to agree with those of Reed in certain important respects. The differences are sufficiently great to cast doubt on whether the two accounts refer to the same mutant.

Reed's waved-2 mice were segregating for albino; no further information on their genetic constitution was given, and no linkage information was available. Control, non-waved-2 hairs were taken from litter-mates. I examined waved-2 hairs from two stocks of mice: a stock originally built up by Michie (1955) and maintained in this laboratory for the past 10 years, homozygous for *a*, *b*, *p*, *d*, c^{ch}, *vt*, *se* and *wa-2* (stock 1), and a stock maintained by Miss Macrae, homozygous for *s*, *ln*, *b*, *a* and *wa-2* (stock 2). Both stocks had been used extensively for linkage tests, and the position of *wa-2* in linkage group VII (Snell & Law, 1939; Falconer, 1947; Wright, 1947; Carter, 1951) confirmed. The waved-2 gene in stock 2 was derived from mice obtained from R. A. Fisher (Genetics Dept., University of Cambridge) in 1947, and the gene in stock 1 originated from the same source, but had been maintained independently for nearly 20 years. Non-waved-2 hairs were taken from a variety of other stocks.

Hairs were plucked from the mid-dorsal region (as were Reed's) and mounted without further treatment in Berlese's fluid. One hundred to two hundred hairs were mounted in a large drop of fluid, with a coverslip on top. The depth of mounting fluid was such that the hairs were not compressed: this made photography difficult, but allowed the hairs to regain their original orientation. Reed's hairs were mounted in gum damar.

The differences between my observations and Reed's are as follows:

(1) Reed states: 'Mice homozygous for waved may be distinguished from non-waved animals at birth by their shorter vibrissae which are visibly bent and curly.' In our stocks 1 and 2, on the other hand, the vibrissae cannot be distinguished from normal at birth, even by those accustomed to examining neonatal vibrissae.

(2) Reed counted more constrictions per hair in waved-2 than in non-waved-2 hairs. This was mostly due to a smaller proportion of 'guard hairs'; that is, hairs having not more than one constriction (this category includes monotrichs, auchenes and awls, in the terminology of Dry, 1926). The mean number of constrictions in zigzag hairs was increased from 3·6 to 3·8. His observations, together with mine, are summarized in Table 1.

The lower overall number of constrictions in my material may merely reflect a difference in terminology. There is often a constricted area near the root of the hair which I do not regard as a true constriction and have not included in my counts; this was very probably counted as a constriction by Reed. Of more significance, in my material the mean number of constrictions in zigzag hairs was consistently lower, not higher, in waved-2 than in non-waved-2 hairs. The overall mean number of constrictions depends, of course, on the percentage of guard hairs; this was very variable, and may depend on the stage of the hair cycle or the exact region of the body sampled.

Table 1. *Observations on waved-2 and control mouse hairs*

Observer	Genotype of mouse	No. of hairs	'Guard hairs' (%)*	Mean no. of constrictions		Hairs showing 'thickened' constrictions (%)†
				All hairs	Zigzag hairs	
Reed	Waved-2	92	17·4	3·2	3·8	—
	Non-waved	92	37·0	2·4	3·6	—
McLaren	Waved-2 (stock 1, 28 days)	82	19·5	2·2	2·6	34·2
	Waved-2 (stock 1, adult)	72	38·9	1·7	2·6	43·1
	Waved-2 (stock 2, adult)	111	17·1	2·1	2·5	31·4
	Non-waved (stock 1, 28 days)	107	19·6	2·4	2·9	17·8
	Non-waved (stock 1, adult)	108	26·9	2·2	3·0	12·6
	Non-waved (Q strain, albino)	123	29·3	2·2	2·9	7·3
	Non-waved (C57BL × C3H F_1)	161	29·8	2·2	3·0	16·3

* 'Guard hairs' here include monotrichs, awls and auchenes, i.e. all hairs with less than two constrictions.

† Only hairs with constrictions have been included.

(3) Reed attributed the waviness of the waved-2 hairs to the increased number of constrictions. He wrote: '...it was found that each wave of the hair usually coincided with a constriction in the hair at the point of curvature. At the constriction the diameter of the hair has become very small, is a point of weakness and therefore responsible for the curve of the hair.' In contrast, I find that the waves seldom coincide with the constrictions, but are due to a bending of the shaft between constrictions (see Plate 1, figs. 1–3). The septa between air spaces are often incomplete or irregular (Plate 1, figs. 4–7) and the shaft sometimes varies in width. This suggests a defect in keratinization during the period of hair formation.

(4) I have observed constrictions of abnormal appearance which are much more common in waved-2 than in normal hairs, and also more extreme in manifestation. These are termed 'thickened' constrictions in Table 1. Although the medulla narrows, as in a constriction of normal appearance (Plate 1, figs. 8–9), the total width of the hair is maintained more or less constant by a marked thickening of the cortex throughout the constricted region (Plate 1, figs. 10–14). Mrs Monica Trigg (personal communication) has

pointed out to me that this appearance may be due merely to the orientation of the constriction, which appears thickened when viewed in a plane at right angles to its greater diameter. Waved hairs may lie in this orientation more often than do straight hairs. In addition to the effect of orientation, it seems likely that the defect of keratinization responsible for the waving may also lead to a characteristic structural abnormality of the constriction. In any event the appearance is very striking and it seems inconceivable that Reed would not have noticed this phenomenon while counting constrictions, and made some comment on it, had it been present in his material. In contrast, he mentions that in his waved hairs the diameter of the hair becomes very small at the constrictions.

Where 'thickened' constrictions occur, the increased amount of keratin in the cortex leads to increased rigidity in the neighbourhood of the constriction, so that curvature in the waved-2 hairs tends to occur between rather than at constrictions (see Plate 1, figs. 1, 10). This is the opposite of the situation reported by Reed. Reed's conclusions ('We may conclude that the waved coat is different from the normal in two main respects. There are fewer guard hairs in waved animals...and there are more constrictions in the waved hairs') are not borne out by the present study.

Reed's mice probably differed more in genetic background from either of the Edinburgh stocks than these did from each other. This may well have affected some of the characters examined, such as the number of constrictions, and the appearance of the whiskers at birth. A more basic difference is that the waves in Reed's hairs apparently coincided with the constrictions, so that the curly appearance of the coat was attributed to an unusually high proportion of zigzag hairs and hence a larger number of constrictions, while in the present material the waves were entirely distinct from the constrictions. This suggests a different mode of gene action, and can hardly be attributed to background effects. It seems likely that the gene carried by my mice is different from, though possibly allelic to, that studied by Reed.

If the gene used in the present study is not the same as that examined by Reed, when could the substitution have occurred? Snell obtained waved-2 mice from Reed, labelled 'Keeler wavy', in 1935, the same year in which Keeler's original report of the mutant was published (Keeler, 1935). The mice were at once crossed by Snell to shaker-2 and the linkage subsequently established (Snell & Law, 1939). Animals of the homozygous *wa-2 sh-2* stock were supplied to Fisher in 1943, and it was from this source that both the stocks of waved-2 mice maintained in this laboratory originated. It therefore seems almost certain that the present waved-2 gene is the descendant of that supplied to Snell, which was probably that originally reported by Keeler. However, Reed's published description (Reed, 1938) of the hairs of this mutant did not appear till 3 years after *wa-2* was supplied to Snell. It is possible that two waved mutants became confused during this period.

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EXPLANATION OF PLATE

Fig. 1. Three zigzags, an awl (*a*) and an auchene (*b*), from a 28-day-old *wa-2* homozygote (stock 1). Note that the waves in the zigzags do not coincide with the constrictions (arrowed).

Fig. 2. Part of the shaft of a zigzag hair from an adult *wa-2* homozygote (stock 1). The shaft is curved, with the keratinized cortex thicker on the inside than on the outside of the curves.

Fig. 3. Strongly curved tip of a monotrich from a 28-day-old *wa-2* homozygote (stock 1).

Fig. 4. Regular septa in the straight part of a zigzag shaft (stock 2).

Fig. 5. Irregular septa in a curved zigzag shaft, from an adult *wa-2* homozygote (stock 2). The pigment granules show up the irregularities in direction and completeness of the septa.

Fig. 6. Irregular septa (arrowed) in a zigzag hair from an adult *wa-2* homozygote (stock 1). Note that the septa are most irregular at the point of curvature.

Fig. 7. Irregular septa in a zigzag hair from a 28-day-old *wa-2* homozygote (stock 1), at a higher magnification. Several of the septa are incomplete.

Fig. 8. Zigzag hair (stock 1) showing normal constriction. The medulla narrows while the cortex remains of uniform diameter, so that the overall diameter of the hair decreases.

Fig. 9. Zigzag hair (stock 1) showing normal constriction, at a higher magnification.

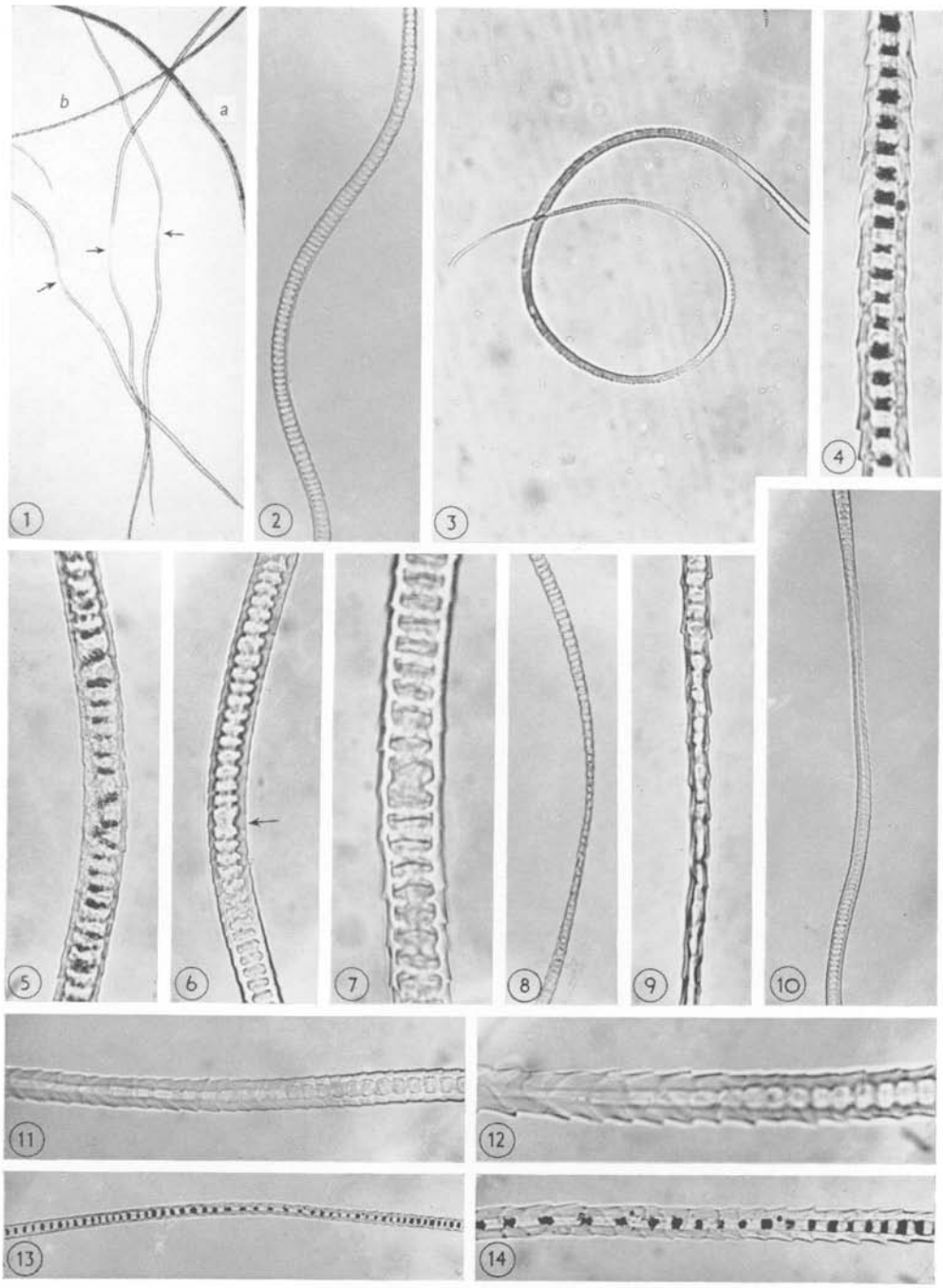
Fig. 10. 'Thickened' constriction in a zigzag hair from a *wa-2* homozygote (stock 1). Note that the hair is straight over the length of the constriction, and the curves lie outside the constriction.

Fig. 11. 'Thickened' constriction in a zigzag hair from a *wa-2* homozygote (stock 1), at a higher magnification. Note that as the medulla narrows, the cortex thickens, so that the overall diameter of the hair changes little if at all.

Fig. 12. As Fig. 11, at a higher magnification still.

Fig. 13. 'Thickened' constriction in a zigzag hair from a *wa-2* homozygote (stock 2).

Fig. 14. As Fig. 13, at a higher magnification.



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(*Facing p.* 260)

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