

STICKY: A NEW MUTANT IN THE GUINEA-PIG

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During the Spring of 1955 a few animals with a defective coat were noticed among the guinea-pigs bred in the Department of Pathology, Cambridge. The affected animals appeared unkempt, ruffled and grubby and felt sticky, as if resin had been rubbed into the coat. For this reason the animals were called "sticky" guinea-pigs.

The defect is most obvious at birth, the new-born young having an extremely sticky coat with enhanced waviness (Pl. 1 Fig. 1). This is particularly noticeable in the offspring of normal mothers who seem unwilling to clean their sticky young. During the first few weeks the stickiness decreases but nevertheless persists throughout life while the waviness disappears completely (Pl. 2, 3 Fig. 2 and 3). The whole coat is affected and food and debris tend to cling to the hair on the muzzle, legs and ventral surface of the trunk (Pl. 4 Fig. 4). Although as judged by their coat, these creatures seem to be in poor condition their appearance is deceptive for they thrive and are robust and healthy. They show no special tendency to skin infections.

The following features suggest that the condition is inherited and is not caused by faulty diet or other environmental factors.

- (a) The first sticky guinea-pigs were the offspring of normal parents and sibs of the sticky animals had normal coats.
- (b) The defect, if present, is always obvious at birth both to sight and touch and persists throughout the life of the affected animal.
- (c) Although living with sticky animals and given the same food, no guinea-pig born with a normal coat has ever become sticky.
- (d) Sticky guinea-pigs are born throughout the year and there is no seasonal variation in their stickiness.

The defect has been investigated genetically and by histological and chemical techniques.

METHODS

a) *Breeding*

The guinea-pigs produced in this Department are used principally for pathological experiments and the main criteria for selecting breeding stock are good health and satisfactory breeding performance. No genetical records are normally kept. Usually

four to six does and one buck are taken from stock and mated together in one large cage. The does are not separated when pregnant and frequently two or more litters are born in the cage at about the same time. During routine breeding, therefore, the mother of any particular animal may not be known.

For the purposes of this investigation does were either kept individually in small cages or separated before parturition if several were housed together. No difficulty in mating sticky with normal animals was experienced even when there was a choice of does in the cage.

(b) *Diet*

The guinea-pigs are normally fed on a well-watered mash with the following constitution :

Beet	30 lb
Bran	14 lb
Oats	14 lb
Fishmeal	$\frac{1}{2}$ lb
Brewer's yeast	$\frac{1}{2}$ lb

Cod liver oil ($\frac{1}{2}$ pint) is added to the mash on one day per week instead of the fishmeal. In addition they are given liberal supplies of greens twice per week and hay once per week. Their bedding consists of oat straw.

To determine whether diet affects stickiness twelve normal and eleven sticky guinea-pigs of both sexes and different ages were given Diet 18 of Bruce and Parkes (1947) for several months in place of the mash. They continued to get greens, hay and oat straw as above.

(c) *Histological*

Fifteen sticky and ten normal guinea-pigs of varying age, sex and coat colour were killed by dislocation of the neck and thorough post-mortem examinations were performed immediately. Pieces of skin from the dorsal and ventral surfaces of the thorax, abdomen and limbs, and blocks of the major organs and tissues were fixed in 4 per cent. formaldehyde in physiological saline. Paraffin sections were prepared and stained by Ehrlich's haematoxylin and eosin, Mallory's phosphotungstic acid haematoxylin, Weigert's resorcin-fuchsin method for elastic tissue and van Gieson's method for collagen fibres and occasionally by Gomori's paraldehyde fuchsin method. Frozen sections of the skin and various organs including the heart, liver, kidneys and spleen were cut and treated with Sudan III and IV or Oil red O.

Hair from many sticky and normal guinea-pigs was examined microscopically both without treatment and after mounting in 20 per cent. sodium hydroxide or in D.P.X.

(d) *Chemical*

Hair was clipped from three sticky and three normal adult albino males. The lipid was extracted from each sample of hair with an ether: ethanol mixture

(9 vol. diethyl ether: 1 vol. ethanol) in a Soxhlet apparatus. The total lipid and saponifiable and non-saponifiable fractions were estimated separately by standard techniques. The iodine number of the fatty acids was determined by Hübl's method.

RESULTS

(a) *Genetical*(i) *Heritable basis*

When three sticky young were noticed among the offspring of five normal does (♀ 1, 2, 3, 4 and 5), the does were removed from the normal buck who had fathered the litters. The does were then mated to a sticky buck (♂ A) which was found in the stock at about the same time. Two does (♀ 1 and ♀ 4) had normal offspring only and two other does (♀ 3 and ♀ 5) produced both normal and sticky young (Table 1) and were

Table 1. *Results of matings of four original does*

♀ (phenotypic normals)	♂ (sticky)	Offspring	
		normal	Sticky
1	A	4	0
3	A	4	2
4	A	6	0
5	A	4	2

the main founders of the sticky stock. The remaining doe (♀ 2) was discarded because she did not breed satisfactorily.

The original three sticky young, two does (♀ 6 and ♀ 7) and a buck (♂ B), were mated together and produced nothing but sticky offspring. One of these does (♀ 7) was later mated to an unrelated normal buck (♂ K), imported from the Ministry of Supply Establishment, Porton Down, Salisbury, and produced only normal offspring (Table 2).

Table 2. *Offspring of first two sticky does*

♀	♂	Offspring	
		Normal	Sticky
6 (sticky)	B (sticky)	0	11
7 (sticky)	B (sticky)	0	8
7 (sticky)	K (normal)	6	0

It was tentatively concluded that sticky is due to a single recessive factor (*st*) and four different types of matings were made to test this hypothesis: namely outcross, intercross, backcross and homozygous sticky (Table 3). The χ^2 and probability values

Table 3. *Results of all breeding experiments in sticky stock*

Type of mating	Expected				Observed				χ^2	Degrees of Freedom	Probability
	Normal		Sticky		Normal		Sticky				
	♀	♂	♀	♂	♀	♂	♀	♂			
Outcross	36.5	36.5	0	0	41	32	0	0	1.109	1	0.30
Intercross*	40.5	40.5	13.5	13.5	40	43	14	11	0.642	3	0.89
Backcross*	50	50	50	50	57	40	56	47	3.880	3	0.27
Sticky × sticky	0	0	68.5	68.5	0	0	68	69	0.007	1	0.93

* Normal guinea-pigs used in these matings were known to be carrying sticky either from their parentage or from previous test-matings.

of the results support the view that sticky is due to a single recessive factor with full penetrance and no appreciable effect on viability or fertility.

(ii) *Linkage*

Stickiness has not been restricted to any one particular coat colour or coat type, such as rosette. On the other hand a loose linkage with one of the coat factors cannot be excluded owing to epistacy within these factors and to the small numbers bred. There is no indication of sex linkage or association with sex. Matings are being made to test linkage with the major colour factors.

(iii) *Deformities*

In the sticky × sticky matings seven deformed animals were found amongst the first ninety nine offspring. These deformities occurred among the young of three does and two bucks whose relationship with one another was uncertain. The deformity consisted of a reduction in the number of toes on the forefeet and persistent flexion of the wrist joint. The two animals surviving to maturity gradually developed a waddling gait, which was associated with malformations of the femur (lateral bowing of the shaft and ventral rotation of the head and neck).

Guinea-pigs with this deformity have not been seen in any other type of matings either in the sticky stock or in the general breeding stock in the Department. With the small amount of information available no conclusions can be drawn about the cause of this deformity and its relationship with sticky.

(b) *Diet*

On Diet 18 of Bruce and Parkes none of the sticky guinea-pigs became less sticky and the coat of the normal animals remained normal. Furthermore, two sticky does, mated to a heterozygous buck, and fed on Diet 18 before and during pregnancy produced one mixed litter containing two normal and four sticky offspring.

As this change to a recognised pellet diet, with added greens and hay, did not affect the degree of stickiness it appears likely that possible deficiencies in the ordinary mash used in the Department are not a factor in the appearance of stickiness.

(c) *Histological*

(i) *Skin and Hair*

No microscopical abnormality was discovered in the skin of sticky guinea-pigs. The structure of the epidermis and dermis appears normal, and no difference between the number, size, structure and fat content of the hair follicles and sebaceous glands of normal and sticky guinea-pigs was detected.

With the ordinary light microscope, hair taken from all parts of the coat of sticky guinea-pigs is of normal dimensions and form when compared with the hair from normal animals. More debris, however, clings to sticky hair than to normal hair, this feature being especially prominent with hair growing on the ventral surface of the thorax and abdomen.

(ii) *Other tissues*

No defect of the cardiovascular, respiratory and nervous systems, of the alimentary and urogenital tracts or of the endocrine glands was found to be associated with stickiness. Similarly, apart from the bone lesions, no defects were discovered in the organs and tissues of the five sticky deformed animals examined.

In the sticky guinea-pigs examined the adipose tissue was normal in quantity, distribution and structure and was not sticky to the touch. Moreover, frozen sections revealed no abnormal accumulations of lipid in the heart, kidneys, liver, spleen, lymph nodes or blood vessels.

(d) *Chemical*

As the microscopical structure of the hair of sticky guinea-pigs appears normal and as the handling of affected animals makes human skin sticky it seemed reasonable to believe that the defect is due to some material on the coat. The fact that stickiness is lost when sticky hair is washed with lipid solvents, such as ether and chloroform, but is unaffected by washing with water suggested that a fatty material was responsible. This belief is supported by the observation that when samples of sticky hair and of normal hair are treated separately, under standard conditions, with a solution of Sudan III and IV in 70 per cent. ethanol and then rinsed with 70 per cent. ethanol, the hair from sticky guinea-pigs has a pronounced orange tinge whereas the hair from normal animals is not stained.

Formal chemical investigation of the hair from three sticky and three normal guinea-pigs revealed that about 4 times as much fat can be extracted from sticky hair as from normal hair (Table 4). An analysis of this fat showed that sticky hair possesses about 2.3 times more non-saponifiable lipid than normal hair and about 7.1 times as much saponifiable lipid. Furthermore, the iodine number of the fatty acids shows that the fatty acid fraction from the sticky hair is more fully saturated than that from normal hair.

Although no structural defect of the sebaceous glands has been discovered in sticky guinea-pigs, the results of this chemical investigation suggest that abnormal sebaceous

Table 4. *Results of chemical analysis of lipid extracted from hair of three sticky and three normal guinea-pigs*

	Normal	Sticky
Total lipid as % of fur	1.2	4.9
Non-saponifiable fraction as % of total lipid ..	67	38
Saponifiable fraction as % of total lipid ..	33	58
Ratio $\frac{(\text{Non sap.})}{(\text{Sap.})}$	2.04	0.66
Iodine number of fatty acids (as g. iodine per 100 g. of fat)	25.9	16.4

secretion is the cause of the stickiness. A more detailed analysis of the lipids present on the hair and an examination of the lipids in the skin and other parts of the body are planned.

SUMMARY

Stickiness of the coat has been observed in some guinea-pigs bred in the Department of Pathology, Cambridge. The condition has been found to be controlled by a single recessive factor with full penetrance and no effect on viability or fertility. Chemical investigation has shown that an excessive amount of lipid is present on the hair. The composition of the lipid differs from that on normal hair. No structural defect of the hair or skin has been discovered and no abnormality of the major organs has been found.

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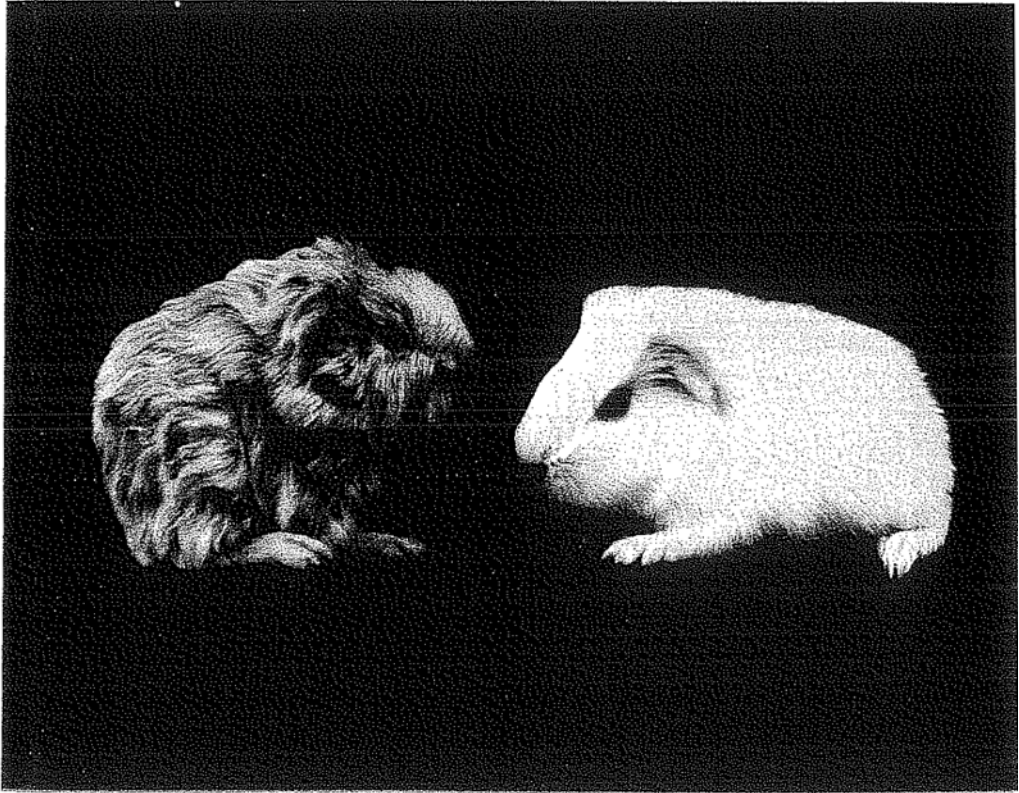


Fig. 1. Two pink-eyed white guinea-pigs (littermates, 22 to 24 hours old)
Left: sticky
Right: normal

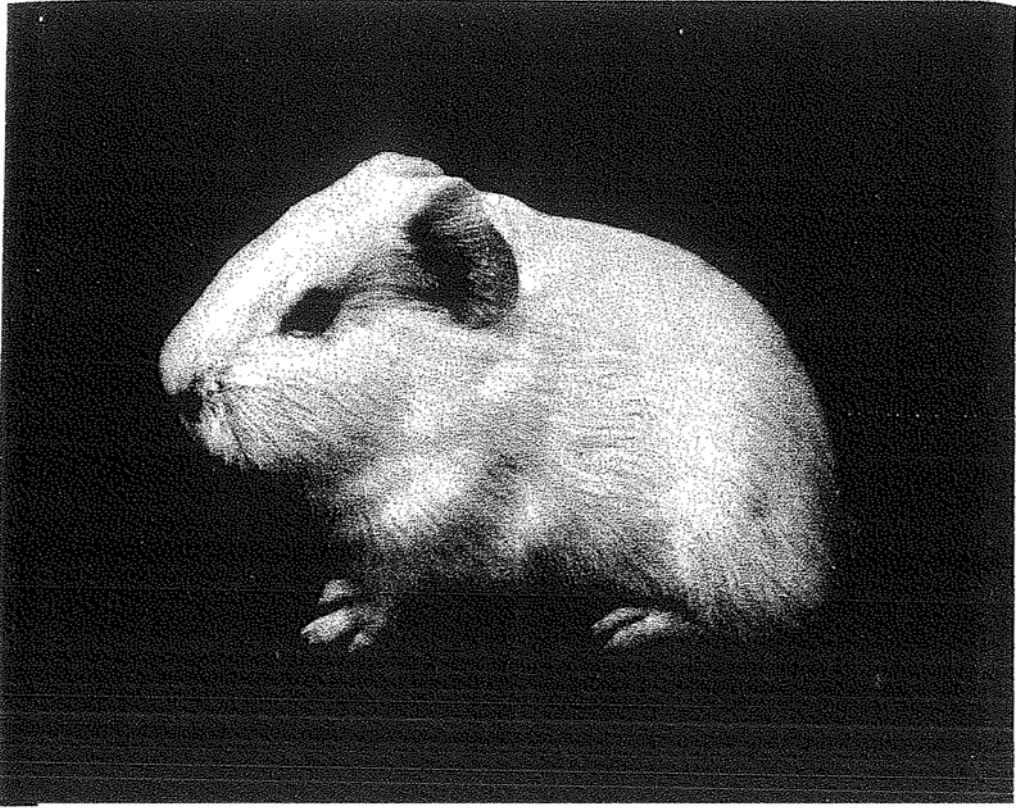


Fig. 2. Normal black-eyed white guinea-pig (about 1 week old).



Fig. 3. Sticky black-eyed white guinea-pig (about 1 week old).



Fig. 4. Two pink-eyed white guinea-pigs (adults)

Left: sticky buck

Right: normal doe