A comparative study of the mechanisms by which X-irradiation and genetic mutation cause loss of vibrissae in embryo mice

By C. M. JACOBSON

From the Department of Zoology, School of Biological Sciences, University of Sydney

INTRODUCTION

It has long been known (e.g. Warkany & Schraffenberger, 1947; Wilson, 1949; Russell & Russell, 1954; Russell, 1957) that X-irradiation can phenocopy mutation and that in mice (Russell, 1950) there are sensitive periods during embryonic development for the production of these effects. It has also been known (Van Scott & Reinertson, 1957) that X-irradiation of adult mouse hair follicles during the active growth phase can cause degeneration. Another group of workers (Fraser & Hall, 1958; Dun, 1958; Kindred, 1964) have produced reductions in the number of facial vibrissae by irradiating random-bred foetal mice with acute doses of 200 r. In these last experiments vibrissa development was only disturbed if the dosage was given between 11 and 13 days of foetal life. Fraser & Hall (1958) have also altered vibrissa number in an apparently similar manner by the introduction of the Tabby gene into a previously random mouse stock. The initial effect of the gene was to cause reduction of vibrissa number and increase of variance, but by further selective breeding of the variant animals both increase and decrease of vibrissa number were produced in Tabby individuals and in their non-mutant sibs (Dun & Fraser, 1959).

The development of facial vibrissae in mice has been investigated by Grüneberg (1943), Rawles (1947), Falconer, Fraser & King (1951), Davidson & Hardy (1952), Dun (1959) and others. These workers have made observations on the timing of initiation and on the process of development in normal mice and in several mutants with abnormal vibrissae. However, the only detailed study is that of Davidson & Hardy (1952), who have divided normal vibrissa development into eight stages, calling the first histological differentiation of the epidermal follicle rudiment stage 1 (each rudiment is composed of an epidermal follicle and a dermal papilla) and the emergence of the hair at the surface approximately 5 days later stage 8 (Text-fig. 1). The facial vibrissae of mice are divided

1 Author's address: Department of Zoology, School of Biological Sciences, University of Sydney, N.S.W., Australia.
Text-fig. 1. Diagrammatic representation of comparative stages in normal (N), regenerating (R), and degenerating (D) vibrissae. X, Irradiated; L, variant lines. Normal stages after Davidson & Hardy (1952).

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th></th>
<th>R</th>
<th></th>
<th>D</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>L</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Text-fig. 2. Head of mouse showing distribution of vibrissae. S-O, supra-orbital group; P-O, post-orbital group; P-Or, post-oral group; I-R, inter-ramal group; M, mystacial group;
Loss of vibrissae in mice

into five groups (Text-fig. 2). Four of these are known as the secondary vibrissae and comprise four supra-orbitals, two post-orbitals, four post-orals and three inter-ramals. The remaining group is that of the mystacials, also called the primary vibrissae. There are about forty-eight of these. In contrast to the secondaries, some variation in numbers in this last group is normal. The time of origin of follicle rudiments varies from group to group. It is 12 days for the supra-orbitals, 12 days for the post-orbitals, 13 days for the post-orals and inter-ramals, and either 12, 13 or 14 days for the mystacials, depending on their position. In the experiments of Fraser & Hall referred to above it is apparent that the effect of X-irradiation only occurred at a certain sensitive stage in early development.

The main purpose of the present study is to determine whether the vibrissa loss produced by irradiation is a true phenocopy of the genetically produced one; i.e. whether disruption of the normal system of development occurs at the same point and in the same manner in both, and whether the two injuries complement each other or are antagonistic.

It is obvious that precursory processes must precede the histological emergence of each follicle rudiment. Work by Rawles (1947) and Hardy (1951) has shown that actual vibrissa site determination in the epidermis occurs at about 8 days. It has therefore been found useful to introduce a stage 0 in addition to the stages of Davidson & Hardy. It is defined as occurring 24 h preceding histological initiation of the epidermal follicle.

MATERIALS AND METHODS

Three series of investigations were undertaken. In the first, 220 embryos were obtained from random-bred females which had been irradiated with 200 r at 8–14 days after vaginal plug formation, i.e. during the known period between vibrissa site determination and hair follicle initiation. Embryos were collected at 24 h intervals after irradiation, providing a series of specimens ranging in age from 9 days to birth (at 21 days), irradiated at different stages of vibrissa development. Irradiation was carried out in rectangular Perspex containers exposed to KVP at a dosage of 38 r/min at 10 in. from the target. The filters were copper. Half of the dosage was given to each side of the body.

In the second series forty-eight embryos from four variant lines carrying Tabby were collected at 24 h intervals from 12 days to birth. These lines, which were selected from many established by Fraser in the Division of Animal Genetics at Ryde of C.S.I.R.O., were:

H.B., A line with extra supra-orbitals.
L.B., A line with a normal vibrissa number, but obtained by selection for low vibrissa number from a line which carries extra supra-orbitals.
H.St., A line with extra supra-orbitals and occasionally extra inter-ramals.
L.St., A line which lacks some vibrissae usually among the inter-ramals but sometimes among the supra-orbitals.
In the third series fifty-five embryos from the same four variant lines were subjected to the same irradiation technique as that used on the random-bred embryos. Exposure was carried out at 12 and 13 days, and the embryos collected at 24 h intervals from 13 to 20 days.

The material obtained in all three series was fixed in formol saline immediately after removal from the uterus, and embedded in 56 °C M.P. paraffin. Sections were cut at 8 µ and stained with Delafield’s haematoxylin and eosin. The vibrissa groups examined were supra-orbitals, post-orbitals, post-orals and inter-ramals.

RESULTS

(1) X-irradiated random-bred mice (Table I)

Before 11 days X-irradiation has no effect on vibrissa number. At 11 days there is occasional loss of a supra-orbital. The greatest effect occurs at 12 days when there is loss of some supra-orbitals, post-orbitals, inter-ramals and occasionally post-orals. At 13 days there are smaller losses of supra-orbitals and post-orbitals and greater losses of inter-ramals and post-orals. After 13 days there is again no effect. Comparison with normal development shows that the different responses are correlated with the time of onset of stage 0, and that the sensitive period extends from stage 0 to stage 3, being greatest at stage 1.

Table 1. Effect of X-irradiation at various foetal ages on total vibrissa number in random-bred mice (total 212 animals)

<table>
<thead>
<tr>
<th>Age irradiated (days)</th>
<th>No. irradiated</th>
<th>No. mice, showing each vibrissa number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>19</td>
</tr>
<tr>
<td>8</td>
<td>11</td>
<td>9</td>
</tr>
<tr>
<td>9</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>10</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>11</td>
<td>38</td>
<td>33</td>
</tr>
<tr>
<td>12</td>
<td>65</td>
<td>10</td>
</tr>
<tr>
<td>13</td>
<td>39</td>
<td>37</td>
</tr>
<tr>
<td>14</td>
<td>33</td>
<td>33</td>
</tr>
</tbody>
</table>

The pattern of damage revealed histologically is identical irrespective of the group to which the vibrissa belongs and varies according to the stage at which irradiation is imposed (Text-fig. 1). Following irradiation at stages 0, 1, 2 and early stage 3, the rudiment degenerates completely. Following irradiation at late stage 3 the rudiment is injured but regenerates (Plate 1, figs. A–D). In cases of complete destruction the first indication occurs about 24 h after irradiation with breakdown of the epithelial follicle to form a ball of disorientated cells which then slowly disintegrate. At the same time the ball of cells sinks into the dermis and its connexion with the epidermis is broken. The epidermis reforms above it about 5 days after irradiation. During the first 3 days after irradiation, in spite of
the follicle disintegration, the dermal papilla proceeds to develop normally. A split then appears between the follicle ball and the papilla. The split spreads round the follicle ball, separating it completely from the surrounding cells by 6 days, and its slow disintegration continues. By the time of birth it has disappeared. Following formation of the split, and beginning about 5 days after the irradiation, the cells of the dermal papilla become disorientated and progressively disperse into the surrounding dermis (Plate 1, fig. C). This process is not completed by the time of birth. At no stage is disintegration of dermal papilla cells observed. Partial degeneration resulting from irradiation at late stage 3 begins when the follicle has reached a length of about 20 μ, has developed a columnar epithelium and has made contact with the dermal papilla. Contact is maintained but the epithelial cell membranes appear to break down. Then, following a quiescent period of about 24 h, cell membranes are again clearly visible in the follicle and development proceeds. It differs from normal in several ways (Plate 1, fig. D). For the first 24 h development is retarded but then accelerates to greater than normal rate. At birth, the hairs so formed are shorter than normal. As part of the early period of very slow growth (stage 4) the hair cone cells are somewhat irregular but attain normal orientation when development becomes rapid at the onset of stage 5. The hair produced, however, is thin and wavy, in contrast to the normal vibrissa which is thick and straight.

In contrast to the constancy in the pattern of damage and in the period of sensitivity, the incidence of response to irradiation is highly variable. In any one group of vibrissae and in any individual mouse only certain vibrissae are affected, and these can differ in every case. Adjacent vibrissae remain normal. Thus there is no correlation of sensitivity with position in a group pattern.

(2) Variant lines of mice (Table 2)

The development of vibrissae in the lines studied proceeded as follows:

(A) In H.B. (Plate 2, fig. E) vibrissa rudiments appear at the normal time and in the normal arrangement except in the supra-orbital group. Here the two standard rudiments on each side have an early developmental delay of 24 h, progressing from stage 1 at 12 days to stage 2 at 14 days. During this time extra rudiments develop ventral to the standard pair, attaining stage 1 by 14 days. Further development of all rudiments proceeds normally but the standard ones remain about 24 h behind the developmental rate of random-bred mice, and are consequently short at birth. The extras, in contrast, accelerate development between 15 and 18 days to become identical with the standard ones by birth.

(B) In L.B. (Plate 2, fig. F) an extra supra-orbital rudiment develops on either one or both sides at 12 days in consort with the standard vibrissae. While the remainder proceed to develop normally, the extra rudiment after attaining stage 2 at 13 days begins to sink into the dermis at 14 days. Although it proceeds to stage 4 at 15 days and a small, abnormal hair cone is formed within it, the rudi-
ment as a whole loses its connexion with the overlying epidermis by 16 days. By 19 days it has become separated from the surrounding dermis. By the time of birth it has usually been fully absorbed. It is notable that the onset of sinking of the follicle coincides with the onset of an abnormality in the dermal papilla. At 14 days the cells of the papilla are no longer tightly clumped, and papilla growth ceases. At 20 days, following separation from the follicle, the papilla cells begin to disperse back into the surrounding dermis.

(C) In H.St. development of the extra vibrissae is indistinguishable from nor-

Table 2. Comparison of developmental stages of vibrissae under different conditions

<table>
<thead>
<tr>
<th>Normal Stage</th>
<th>Regeneration after 200 r at 12 days</th>
<th>H.B.</th>
<th>L.B.</th>
<th>H.St.</th>
<th>L.St.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>5</td>
<td>6</td>
<td>6</td>
<td>D</td>
</tr>
<tr>
<td>7</td>
<td>6–7</td>
<td>6</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>8</td>
<td>7–8</td>
<td>7</td>
<td>8</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

N, Normal vibrissa; E, extra vibrissa; D, degenerating vibrissa; A, additional vibrissa in L.St. which degenerates; S-O, supra-orbital; I-R, inter-ramal.

The first column shows normal development divided into eight stages. Later columns show the relative effects of various conditions in retarding and stopping development (see also Text-fig. 1).

EXPLANATION OF PLATES

D, Degenerating supra-orbital vibrissa; DF, degenerating follicle; DI2, degenerating inter-ramal vibrissa at stage 2; DI5, degenerating inter-ramal vibrissa at stage 5; DP, degenerating papilla; EC, empty hair canal; F, follicle; H, hair; HC, hair cone; N, normal supra-orbital vibrissa; NI, normal inter-ramal vibrissa; P, papilla.

PLATE 1

Fig. A. T.S. of basal region of normal vibrissa at 16 days, stage 6. The hair can be seen in the centre of the hair canal in the centre of the follicle. × 600.

Fig. B. L.S. of two supra-orbitals at 18 days. The one on the left is at stage 7–8 with the hair just emerging. The one on the right is degenerating. The specimen was irradiated with 200 r at 12 days. × 150.

Fig. C. T.S. of a degenerating supra-orbital at 17 days after irradiation with 200 r at 12 days. No hair has formed and the follicle cells are split and disorientated. The papilla cells are just commencing to disperse on the upper edge. × 600.

Fig. D. L.S. (somewhat lateral) of a regenerating supra-orbital at 18 days, stage 5, after irradiation with 200 r at 12 days. The hair cone is beginning to elongate, but the canal has not yet formed. There is no papilla disorganization, and the follicle is fairly normal. × 250.
Loss of vibrissae in mice

They are spaced as extensions of the basic pattern and show neither acceleration nor retardation of growth.

(D) In L.St. (Plate 2, figs G, H) vibrissa development proceeds normally until 16 days. Some rudiments then remain arrested at stage 2, and slowly degenerate by splitting off of the follicle from the papilla, resorption of follicle cells and dispersion of papilla cells. Disintegration is slow, with papilla dispersion only just beginning at birth.

(3) X-irradiated variant lines of mice (Table 3)

After exposure of the lines to 200 r at 12 and 13 days, the following effects occurred:

(A) In H.B., irradiation affects only the supra-orbital group. The standard rudiments react as in random-bred mice. After irradiation at 12 days (stage 1) they show either complete degeneration or no response. After irradiation at 13 days (early stage 2) they show a few examples of degeneration but otherwise remain unaffected. The extra supra-orbitals react differently. After irradiation at 12 days (stage 0) they show either partial degeneration or no response. After irradiation at 13 days (stage 1) they show a high incidence of partial degeneration but only a few instances of total degeneration.

(B) In L.B. irradiation at 12 or 13 days has no effect on the course of development and subsequent degeneration of the extra supra-orbital rudiment. Irradiation at 12 days causes the standard vibrissae to show occasional examples of either complete or partial degeneration, and at 13 days a very few examples of partial degeneration only.

(C) In H.St. irradiation affects the supra-orbital and inter-ramal groups in a different manner from that in random-bred mice. At 12 days the supra-orbitals (stage 1) show no complete degeneration of either standard or extra rudiments but all are retarded in development by about 24 h. The inter-ramals (stage 0) are similarly retarded. After irradiation at 13 days the supra-orbitals (stage 2) show similar retardation of standards and extras plus a few instances of complete degeneration. The inter-ramals (stage 1) show only retardation.

(D) In L.St. irradiation at 12 or 13 days causes the sensitive inter-ramals

---

Plate 2

Fig. E. L.S. of an extra supra-orbital in the H.B. line at 18 days. Although retarded in development, it is normal. x 150.

Fig. F. L.S. (slightly lateral) of a degenerating supra-orbital of the L.B. line at 25 days, stage 4. The hair cone and the follicle are breaking down, and the connexion to the overlying epidermis is about to disintegrate. x 400.

Fig. G. T.S. of basal region of degenerating inter-ramal of the L.St. line at 16 days. There is no hair cone, and papilla disorientation is evident. Compare Plate 1, fig. A. x 600.

Fig. H. L.S. of inter-ramals of the L.St. line at 17 days. The uppermost one is degenerating, the middle one is normal (stage 7) and the lowermost one is retarded (stage 2). x 400.
(stage 0 or 1) and supra-orbitals (stage 1 or 2) to degenerate more quickly than usual, so that they disappear by 17 days. The mode of degeneration remains the same. The rudiments of all other vibrissae, in contrast, show less degenerative response than for random-bred mice treated similarly.

Table 3. Effect of X-irradiation of 200 r on vibrissae of mice of the variant lines

<table>
<thead>
<tr>
<th>Line</th>
<th>Group</th>
<th>X at 12 days</th>
<th>X at 13 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>R  D  N</td>
<td>R  D  N</td>
</tr>
<tr>
<td>H.B.</td>
<td>S-O</td>
<td>32% 68% 4%</td>
<td>96%</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>40  60 20 20</td>
<td></td>
</tr>
<tr>
<td>L.B.</td>
<td>S-O</td>
<td>10 14 56 38</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>P-O</td>
<td>10 20 70 60</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>P-Or</td>
<td>15 85 35 40</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>I-R</td>
<td>10 90 58 42</td>
<td></td>
</tr>
<tr>
<td>H.St.</td>
<td>S-O</td>
<td>100 81 19</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>100 100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>I-R</td>
<td>83 17 67 33</td>
<td></td>
</tr>
<tr>
<td>L.St.</td>
<td>S-O</td>
<td>11 89 12</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>P-O</td>
<td>17 83  100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P-Or</td>
<td>100 100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>I-R</td>
<td>15 85 25 75</td>
<td></td>
</tr>
</tbody>
</table>

R, Retarded vibrissa; D, degenerated vibrissa; N, normal vibrissa; S, standard vibrissa; E, extra vibrissa; S-O, supra-orbital group; P-O, post-orbital group; P-Or, post-oral group; I-R, inter-ramal group.

DISCUSSION

Irradiation sensitivity to 200 r exists in the vibrissa rudiments of random-bred mice between stages 0 and 3. The majority of rudiments show no response before late stage 3 but some, the actual number of which is variable, completely disintegrate. Reasons for this 'all or nothing' reaction and for the mechanism which always preserves some vibrissae intact are unknown. The response at late stage 3 is also variable, but if it occurs it causes only partial degeneration followed by recovery. Complete degeneration is always associated with separation from the dermal papilla, which then disperses. Recovery occurs when contact with the papilla is not lost. There are indications in this of follicular evocation of papillar aggregation and subsequent papillar evocation of continuation of follicular development. Dermal evocation of epidermal morphogenesis has often been described (e.g. Montagna, 1956, 1961) but the possibility of an earlier reverse process has not.

In the cases of genetically induced vibrissa loss (L.B. and L.St.) rudiment
Loss of vibrissae in mice 377
degeneration begins with early abnormality of the dermal papilla and then follows a similar course to that produced in response to irradiation. Whether selection has occurred for abnormality of the follicle–papilla evocator or for the papilla–follicle evocator or for both is not clear, but both the genetic vibrissa loss and the irradiation effect which phenocopies it act on the same period of epigenetic crisis, i.e. the period of interaction between two independently derived rudiments. At this point, both through environmental stress and genetically in the L.St. line, one may consider that the lower threshold of canalization of the secondary facial vibrissa system is broken, resulting in number reduction and increased variance. However, the significance of this epigenetic crisis in the L.B. line is different and must be considered with the results for H.B. and H.St. lines.

In the two high lines, which combine an increase in vibrissa number and variance, canalization is broken at the upper threshold. This has been achieved by selection acting through genetic control of the initial formation of vibrissa sites. Only the number of sites is increased. Vibrissa development is normal except for a slight delay in the supra-orbitals of the H.B. line. The period of site determination is therefore an epigenetic crisis at which canalization can be disrupted. The evidence from the L.B. line, however, suggests that the lower threshold is stronger than the upper. L.B. combines vibrissa number reduction with a decrease in variance, selection having resulted in a return to the random-bred level. This has occurred not by elimination of the extra vibrissa site produced through previous selection but by new selection on the epigenetic crisis which is important in L.St. and in irradiated animals.

Three general conclusions can be drawn from these data:

1) Two epigenetic crises exist in vibrissa development, one at the time of site determination, in which a mechanism acts to limit the number of sites, and the other at the time of follicle–papilla interactions, at which a mechanism operates to promote full expression of the already determined sites. The first is probably a type of limited field (Waddington, 1962). The second is probably a mechanism underlying evocator action between follicle and papilla.

2) In terms of the canalization theory, the upper and lower thresholds have been broken by selection acting independently on these two mechanisms, the upper by breaking control of the field, the lower by breaking control of the follicle–papilla interaction.

3) The reintroduction of the random-bred level in the L.B. line has not restored the original control of the limited field, but has introduced a new canalization mechanism operating on the second epigenetic crisis in the extra vibrissa.

The results obtained by exposing the animals of the variant lines to X-irradiation support these conclusions. Both H.B. and H.St are more resistant to irradiation than random-bred mice. This suggests a stronger determination of follicle rudiments through more powerful operation of the determination field. In L.St., degeneration of rudiments is more rapid, confirming that follicle–papilla
interaction (on which irradiation acts) has already been weakened by selection as suggested. In L.B., response to irradiation is identical to that of random-bred mice, confirming recanalization.

**SUMMARY**

1. Both X-irradiation and certain genetic mutations can produce loss of vibrissae in mice.
2. The aim of this investigation was to determine whether disruption occurred at the same point in development and in the same manner.
3. Histological investigation was made of vibrissae during early stages of development.
4. It was found that two periods of epigenetic crisis exist in vibrissa development, one at the time of site determination and the other at the time of follicle–papilla interaction when development has just been initiated.
5. Irradiation damage acts by disrupting this follicle–papilla interaction. If the contact is broken in the very early stage, the vibrissa will degenerate. If irradiation acts a little later, when the cells are less sensitive, the contact is not broken, and the vibrissa follicle cells will recover from the damage and continue to develop.
6. In one mutation studied, the same interaction was destroyed because there was a genetic abnormality in the papilla. This produced the same ultimate effect as did irradiation.
7. In other cases, the mutation acted on the first crisis, affecting the site determination. Here, although the apparent effect was the same as in irradiation, the mechanism differed.

**RÉSUMÉ**

*Étude comparative des mécanismes par lesquels l'irradiation aux rayons X et la mutation génétique provoquent la perte des vibrisses chez l'embryon de souris*

1. Une irradiation aux rayons X et certaines mutations génétiques peuvent provoquer la perte des vibrisses chez la souris.
2. Le but de ces recherches a été de déterminer si l’anomalie s’est produite au même stade de développement et de la même manière.
3. On a fait l’étude histologique des vibrisses au cours des premiers stades du développement.
4. On a trouvé qu’il existe deux périodes de crise épigénétique dans le développement des vibrisses, l’une au moment de l’interaction entre follicule et papille, quand le développement vient juste de commencer.
5. L’irradiation agit en rompant cette interaction entre follicule et papille. Si le contact est interrompu, au stade le plus précoce, la vibrisse dégénérera. Si l’irradiation agit un peu plus tard, quand les cellules sont moins sensibles, le contact n’est pas interrompu, les cellules du follicule de la vibrisse survivront et continueront à se développer.
6. Dans une des mutations étudiées, la même interaction a été supprimée par suite d’une anomalie génétique de la papille. L’effet ultime a été le même que celui de l’irradiation.

7. Dans d’autres cas, la mutation agissait sur la première ‘crise’, affectant la détermination de l’emplacement. Ici, bien que l’effet apparent fut le même que celui de l’irradiation, le mécanisme en était différent.

I am very grateful to Dr D. T. Anderson for his advice in the preparation of this manuscript and for the facilities provided by Professor A. S. Fraser and Dr J. M. Rendel at the Division of Animal genetics, C.S.I.R.O. I also wish to thank Mr I. Bradshaw for photographic assistance.

REFERENCES


(Manuscript received 8 November 1965, revised 28 March 1966)