A MOSAIC (DARK-EYED INTENSE—PINK-EYED DILUTE) COAT COLOUR OF THE HOUSE MOUSE.[1]

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Numerous cases have been reported in the literature in which individual plants and animals have been mosaics of tissue of two different genetic constitutions. Among insects several cases have been described in *Drosophila* by Mohr (8), Morgan and Bridges (9), and Muller (10); and in *Habrobracon* by Whiting (12), and Whiting and Whiting (13). In mammals a number of individual instances of mosaics are on record. Castle (5) described an intense-dilute mosaic coat pattern in the rabbit which was inherited through three generations. The so-called Japanese variety of rabbit is a mosaic of black and yellow which is inherited as an allelomorph of the black extension series (Castle (4)). Ibsen (7) has pointed out that the tortoiseshell coat of guinea-pigs, a mosaic of black and yellow areas, is also inherited as an allelomorph of the black extension series. In the domestic cat tortoiseshell pattern is a similar combination of black and yellow and occurs frequently in females, rarely in males. It appears as the heterozygous condition of black and yellow. Castle (2) reported on a guinea-pig which appeared to be an albino except for small areas of sepia on the head and hips and dark streaks in the iris. Castle (3) also described a mosaic condition in which intensity and red-eyed dilution were both present in the pelage of a hooded piebald Norway rat. In that instance the unusual coloration was not inherited. A group of interesting cases of mosaic coat patterns of guinea-pigs was reported by Wright and Eaton (14). None was transmitted to later generations. One reported by these authors was unusual in having not only the soma of a mosaic nature but also the germinal epithelium. This case is unique among those reported in mammalian material in this respect.

Mosaic coat colours of several types have been reported in the house mouse. Fisher (6) noted one and Pincus (11) described three mice which were heterozygous for the black-brown pair of allelomorphs and which possessed mosaic coat patterns of black and brown. This unusual condition was not inherited in these mice. A case of a brown mouse with a

[1] Observations reported in this paper were made in the Laboratory of Vertebrate Genetics, University of Michigan.

dilute ventral surface of the coat was reported by Bittner (1). This mouse bred as a dilute brown.[1]

It is proper in this brief review of the literature to note that Castle (5) and Pincus (11) suspected a relation of the mosaics in rabbits and mice respectively which they reported with the presence of white spotting or piebald characters. It seems probable that the rat described by Castle (3) and several of the guinea-pig cases cited above may also have had a relation of the mosaic pattern to white spotting.

The pink-eyed dilute mutation is one of the first which has been described for the house mouse, *Mus musculus*. Its effects upon the colour of the coat, eyes and skin are marked. Practically all of the pigment of the eyes and skin is removed. The wild-type agouti pattern is reduced by this recessive character to a tawny yellow. In combination with non-agouti pink-eyed dilution converts a practically black mouse into one in which the eyes are almost devoid of pigment and the hair is a gull grey. Ample data have demonstrated that the pink-eyed dilution locus is linked with the albino and one of the shaker loci.

In the fall of 1932 two mice appeared among the offspring of one pair of parents which were mosaics of dark-eyed intensity and its allelomorph pink-eyed dilution. One (♂4084) was born on 29 October, 1932, and the other (♀4085) was produced in the following litter on 21 November, 1932. Their parents were hybrids between a pink-eyed self stock and a dark-eyed, piebald, non-agouti stock which also carried dominant, anaemic white-spotting. They were of the composition $\frac{\mathbf{A\ d\ P\ s}}{\mathbf{a\ D\ p\ S}}$ in terms of the symbols for the genes of mice. Their appearance was typical of mice of that composition, that is, wild-type coloration with the exception of a white area on the abdomen about a centimetre in diameter and a small group of white hairs on the nape.

The two mosaic mice were non-agouti. The intense, black areas were clearly defined in contrast with the dilute, gull grey areas. Both showed the small abdominal spot of white which is characteristic of mice

[1] Since this paper was written another very interesting colour mosaic has been reported by L. C. Dunn, *J. Genet.* **29**. In this house mouse about one-tenth of the dorsal area had mutated from full colour intensity to albinism. The mouse was heterozygous for another albino allelomorph, ruby-eyed dilution, which is incompletely dominant over albinism. The mutant areas thus appeared as the heterozygous condition between albinism and ruby-eyed dilution and were in marked contrast with the remainder of full intensity. In this mouse the mutation affected the germ cells also for gametes of three types were produced: ruby-eyed dilute 50 per cent., full colour 40 per cent., albino 10 per cent. Dunn concluded that a mutation in a pregonial cell had produced this unusual condition. The mouse was heterozygous for the recessive piebald gene.

heterozygous for the recessive belt-type of piebald and its allelomorph self-pigmentation. They were beautiful examples of a new tricolour in mice—black, grey and white. The male showed a predominance of the intense, black type of colour. The dilute area consisted dorsally of an irregular belt, averaging a centimetre in width which passed over the back in the lumbar region. Ventrally the dilute area extended from the abdomen to the mouth and nose, and was visible laterally at the axillae. Thus it covered most of the ventral surface. Within it, on the abdomen, was an irregular circular area of white about one centimetre in diameter. The eyes were intense (black). The female's coat was predominantly dilute or gull grey. The intense pigmentation was restricted to small irregular areas around the base of each ear, in the thoracic region of the back, and on the rump near the base of the tail. Their total extent did not exceed five square centimetres. She also possessed a small white area on the abdomen. Her eyes were dilute (almost devoid of pigment).

These two individuals were the only observed mosaics among a total of 53 offspring from their parents. Brothers and sisters of their parents produced 211 offspring among which no unusual colour types were observed. Both of the mosaic mice were bred as extensively as possible. When mated together they produced 13 young. The female was then mated with a pink-eyed piebald son which was sired by ♂4084 and with him produced 31 offspring. The mosaic male produced a total of 174 young when mated with non-mosaic sisters. With his daughters he produced an additional 307 offspring. Careful examinations of each mouse from these several matings failed to reveal the appearance of any additional mosaic coat colours. It may be concluded that the tendency to produce this unusual type of coloration in this stock of mice was not inherited to any large extent.

Although we found no evidence of a strictly inherited tendency of the mosaic nature of these two mice, their breeding performance proved very interesting by further explaining their constitution. It provided a probable series of causes of the peculiar coloration of their pelage. The male bred as a typical mouse homozygous for non-agouti and non-anaemic white-spotting but heterozygous for the black-brown, dark-eyed—pink-eyed and self-piebald pairs of characters. His formula was, therefore, **aa Bb Dd Pp ss**. The female proved to be of identical constitution except that she was heterozygous for the anaemic white-spotting gene. The homozygous state of this gene is lethal. Her formula was **aa Bb Dd Pp Ss**. It is noteworthy in this connection that both of these mice proved to be actually heterozygous for the two states of the

gene which were present in areas of their coats. The usual coat of the mouse heterozygous for dark-eye and its allelomorph pink-eyed dilution is, however, entirely of intense pigmentation. Some agency operated in the two mosaic individuals to permit the normally recessive allelomorph to assert itself in a part of the fur. In ♀4085 the recessive pink-eye factor also determined the pigmentation of the eyes. The coats of these two mice were not entirely of dilute pigmentation, however, for the dominant dark-eyed intensity factor had determined pigment in certain regions. The question arises at once as to what agency or agencies determined the areas in which the normally dominant dark-eyed intensity could assert itself, and conversely, those in which the recessive condition appeared.

The means of explaining the appearance of tissue of recessive type in a heterozygous individual are difficult. The literature suggests several alternative agencies: (1) Mutation of the dominant state of the gene to the recessive state in a cell of an early cell generation of somatic tissue. (2) Faulty mitosis in which part or all of the chromosome bearing the dominant gene is lacking in a cell of an early generation and consequently in its descendants. (3) The acquisition by the gene itself of a mosaic nature which is reflected by the developed character as a similar, parallel, mosaic effect. (4) A temporary reversal of the dominance in certain regions. In the case of the mice under consideration an explanation by assuming the elimination or inactivation of the dark-eyed intensity bearing chromosome, or an aberration or inactivation involving the part carrying this gene in early generations of somatic cells seems most logical. Cytological evidence would be necessary, however, to support this conclusion upon critical examination. Such evidence is unfortunately lacking. Gene mutations seem inadequate for explaining cases of this kind because of the regular appearance of the recessive state of the gene already present in the individual and not a new allelomorph. The particular gene in question here has never appeared to be one of the particularly mutable genes. The failure of the mosaic condition to perpetuate itself in these mice does not favour the assumption that a mosaic condition of the gene arose. The difficulties involved in attempting to explain cases of this sort by assuming a reversal of dominance seem to be very great from the standpoint of the chemistry of development. I am not in a position to recognise that the reactions produced by a colour gene such as this one are reversible.

The explanation of the expression of one condition of the gene and not the other in a particular part of the pelage is also difficult. In the

case of these mice there appeared a marked agreement between the intense areas of their coats and the coloured areas of the coats of mice of the homozygous piebald stock. Each had the white areas which are characteristic of mice of their respective constitutions for the two genes for white areas in a coloured pelage. When to the white area in each pelage were added the dilute areas, the resulting areas were those characteristically white in mice of the compositions **ppss** and **ppSs** instead of **Ppss** and **PpSs**. On the basis of distribution of the dilute parts of the fur the single **P** factor appeared to make the expression of the dilute allelomorph possible in the areas in which it alone was responsible for pigment production. The mosaic condition of the pelage appeared to depend in these mice upon the fact that they were heterozygous for the piebald factor. The presence of one **S** factor in the constitution operated indirectly by giving the single **P** factor control of a larger area of the coat. As a result ♀4085 showed larger dilute areas than did ♂4084. While in both individuals the areas of the coat which were dilute seem to be determined by the single self gene, this does not obtain for the eye. The eyes of ♀4085 were pink, which may be taken to indicate that the dilute gene controlled these organs independently of the piebald gene. These mosaic mice support the view that certain areas of the mouse's coat break down more readily than others to reduced pigmentation. Areas of the second degree in this respect were those in which the dilute gene expressed itself.

SUMMARY.

Two cases of mosaic (dark-eyed intense—pink-eyed dilute) pelage patterns are reported in the house mouse. The unusual colour was not inherited by descendants. A direct correlation between the mosaic pattern of the coat and the pattern of piebald white-spotting in this strain of mice was observed. Aberrant chromosome division in somatic tissue is suggested as an explanation of these mosaics.

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