CHAPTER V

THE ORIGIN OF MUTANT CHARACTERS

THE modern study of heredity has been intimately bound up with the origin of new characters. In fact, the study of Mendelian inheritance is possible only when there are pairs of contrasted characters that can be followed. Mendel found such contrasted characters in the commercial stocks that he used, tall and short, yellow and green, round and wrinkled peas. Later work has also extensively used such material, but some of the best material is supplied by new types whose origin, in pedigree cultures, is better known.

These new characters arise for the most part suddenly, fully equipped, and maintain their constancy in the same way as do the characters in the original type from which they arose. For example, the white-eyed mutant of Drosophila appeared in a culture as a single male. When mated to a common red-eyed female, all the offspring had red eyes (Fig. 38). These were inbred and produced in the next generation red-eyed and white-eyed individuals. All the white-eyed individuals were males.

These white-eyed males were then mated to different red-eyed females of the same generation. Some of the pairs produced equal numbers of white-eyed and red-eyed offspring, both males and females. When the white-eyed individuals were bred together they gave rise to pure white-eyed stock.

We explain these results in accordance with Mendel's first law, which postulates a red-producing and a white-producing element (or gene) in the germinal material.

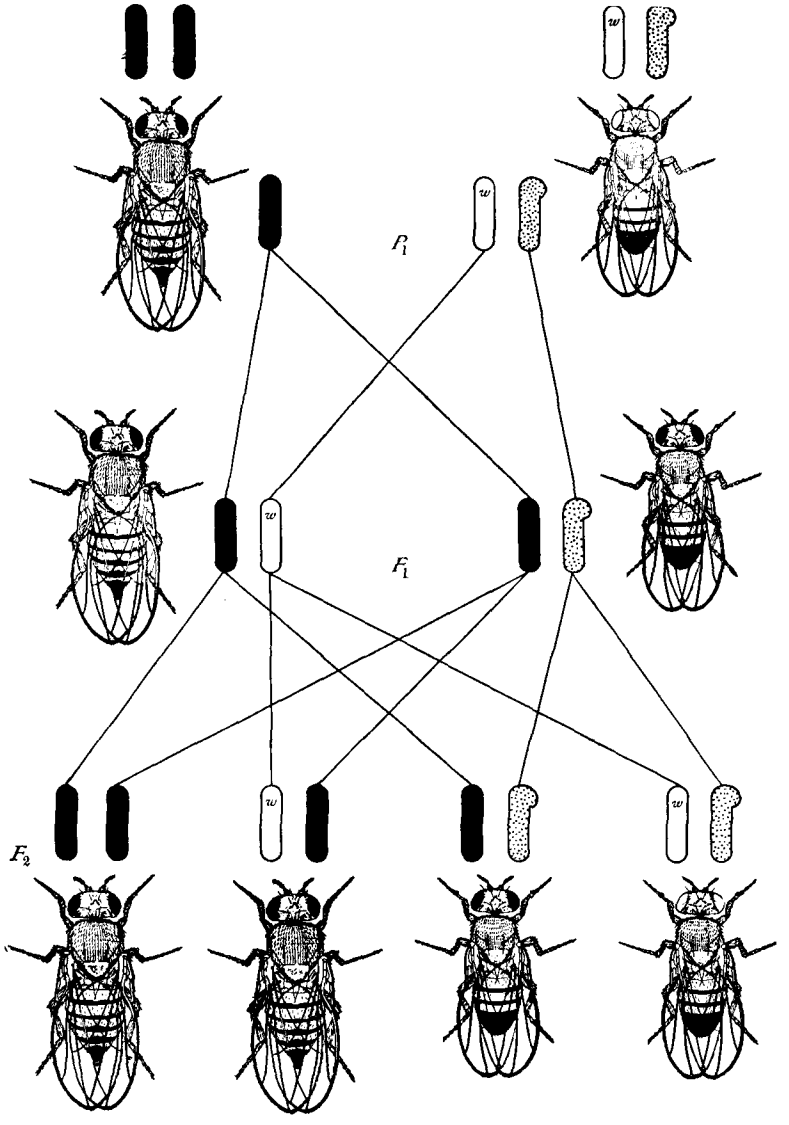

FIG. 38.

Sex-linked inheritance of white eyes in D. melanogaster. A white-eyed male is bred to a red-eyed female. The X-chromosome carrying the gene for red eye is represented by the black rod; the X-chromosome carrying the gene for white eyes is represented by the open rod, and the white recessive gene carried in the chromosome, by small w. The Y-chromosome is stippled.

They behave as a pair of contrasted elements, that are separated in the hybrid at the maturation of the eggs and sperm.

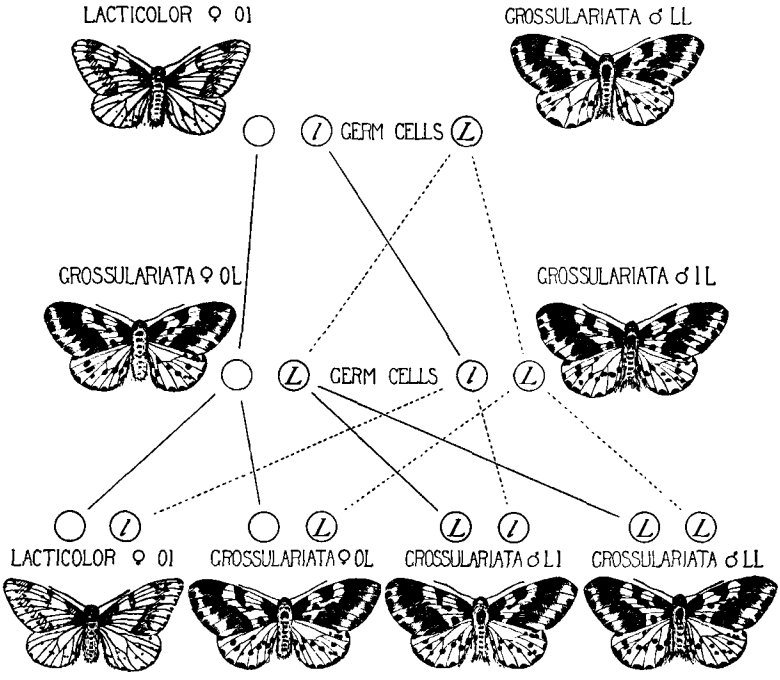

FIG. 39.

Diagram showing a cross between the light-colored type (lacticolor) of Abraxas and the common or dark type (grossulariata). The sex-chromosome carrying the gene for dark color is here indicated by the circle enclosing L, that for light color by the circle with l. The open circle (without an included letter) stands for the W-chromosome that is confined to the females.

It is important to observe that the theory does not state that the white-eyed gene alone produces white eyes. It states, only, that a change took place in some part of the original material, and in consequence of this single change, the material, taken as a whole, now gives rise to

a different end-product. In fact, the change not only affects the eyes, but other parts of the body as well. The sheath of the testes is colorless, while it is greenish in red-eyed flies. The white-eyed flies are more sluggish than their red-eyed fellows, and have a shorter life. It is probable that many parts of the body are affected by the change that took place in some part of the germinal material.

At rare intervals, lighter colored, or pale individuals, of the currant moth, Abraxas, appear in nature. They are females as a rule. A pale, mutant female bred to a dark, wild type male (Fig. 39) gives offspring that are

FIG. 40.

The mutant character Lobe^2 of D. melanogaster. The eyes are small and protruding.

like the dark type. These, inbred, give the old and the new types as 3 to 1. Pale F_2 individuals are all females. If they are bred to males of the same generation, some pairs give pale males and females, as well as dark types in equal numbers. From the former a pale stock can be reared.

The two preceding mutant characters act as recessives toward the corresponding character in the wild type, but other mutants act as dominants. For example: *lobe*^{2} is characterized by the peculiar shape and size of the eye (Fig. 40). It arose as a single individual. Half of its off-

spring showed the same character. A change in a gene in one of the second chromosomes must have taken place, either in the mother or father of the mutant. The germ-cell containing this gene met a cell containing a normal gene at the time of fertilization, and the first mutant arose. The first individual was, therefore, hybrid or

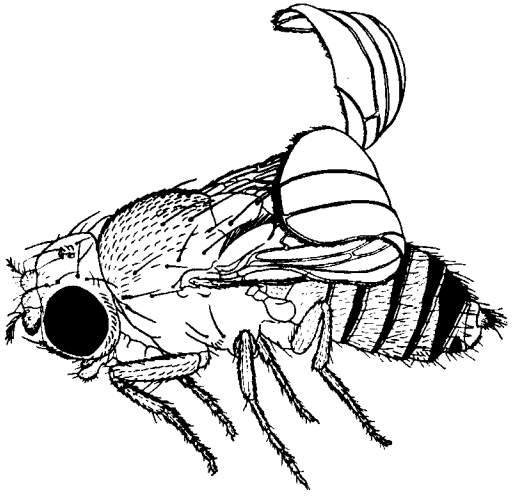

FIG. 41.

The mutant character Curly of D. melanogaster. The wings curl up at the ends and are held somewhat apart.

heterozygous, and, as stated above, produced, when mated to a normal individual, both lobe[2] and normal offspring in equal numbers. From these heterozygous forms some pure lobe[2] flies were produced by mating two lobe[2] individuals. The pure type (homozygous for lobe[2]) resembles the heterozygous type, but the eyes are often smaller, and one or both may be absent.

It is a curious fact that many dominant mutants are lethal in homozygous conditions. Thus curly wing (Fig. 41), a dominant character, nearly always dies when homo-

zygous. Rarely, however, an individual survives. The mutant, yellow coat-color in mice, is lethal as double dominant, as is also the mutant gene for black-eyed white in mice. In all types of this sort, pure breeding stock cannot be produced (except by "balancing" the dominant with another lethal). They produce, in each generation, individuals like themselves and some other type (the normal allelomorph) in equal numbers.

The short-fingered or brachydactyl type in man is a striking dominant character whose inheritance is well known. It will hardly be questioned that it arose as a dominant mutant that established itself in certain families.

All the stocks of Drosophila have arisen as mutants. In the cases that I have given the mutant first appeared as a single individual. In several other cases, however, the new mutant type first appeared in several individuals. In such cases the mutation must have appeared early in the germ-track, so that several eggs or sperm-cells came to carry the mutated element.

At other times a quarter of all the offspring from a pair are mutants. These mutants are recessives, and the evidence shows, in such cases, that the mutation had occurred in an ancestor, and, being a recessive, it did not appear on the surface until two individuals each having the mutated gene met. A quarter of their offspring are then expected to show the recessive character.

Closely inbred stocks are expected to give this sort of result more often than outbred stocks. If outbred, the recessive gene may be distributed to a large number of individuals before two such individuals meet by chance.

It is probable that there are many concealed recessive genes in the human germ-material, since some defective characters recur oftener than expected by independent mutation. When their pedigrees are traced they often

show relatives or ancestors with the same mutant character. Human albinos furnish, perhaps, the best example of this sort. In many cases they come from stocks both of which carry the recessive gene, but it is always possible that a new gene for albinos may have been produced by mutation. Even then it cannot come to expression until it meets another like gene.

Most of our domesticated animals and plants show characters that behave in inheritance in the same way as do the mutants whose origin is established. There can be no reasonable doubt that many of the characters have arisen by sudden mutations, especially in cases where the domesticated types have come from inbred pedigree stocks.

It is not to be inferred from the preceding examples that the production of mutants is peculiar to domesticated races; for this is not the case. There is abundant evidence that the same kinds of mutations occur also in nature. Since most of the mutants are weaker or less well-adapted types than the wild type, they disappear before they are recognized. In cultivation, on the other hand, the individual is protected, and the weaker types have a chance to survive. Moreover, domestic forms, especially those reared for genetic purposes, are carefully scrutinized, and our familiarity with them accounts for the detection of many new types.

A study of the occurrence of mutations in the stocks of Drosophila has brought to light a curious and unexpected fact. The mutational change takes place in one member only of a pair of genes—not in both at the same time. It is difficult to imagine what kind of an environmental effect could cause one gene in one cell to change, and not the other identical gene. Hence it may seem that the cause of the change is internal rather than external. This question will be further discussed later.

TABLE I

RECURRENT MUTATIONS AND ALLELOMORPHIC SERIES

Locus	*Total Occurrences*	*Distinct Mutant Types*	*Locus*	*Total Occurrences*	*Distinct Mutant Types*
apterous	3	1	lethal-a	2	1
ascute	4±	1	lethal-b	2	1
Bar	2	2	lethal-c	2	1
bent	2	2	lethal-e	4	1
bifid	3	1	Lobe	6	3
bithorax	3	2	lozenge	10	5
black	3+	1	maroon	4	1
bobbed	6+	1	miniature	7	1
brown	2	2	Notches	25±	3
broad	6	4	pink	11+	5
cinnabar	4	3	purple	6	2
club	2	2	reduced	2	2
cross-veinless	2	1	rough	2	2
curved	2	2	roughoid	2	2
cut	16+	5+	ruby	6	2
dachs	2	2	rudimentary	14+	5+
dachsoid	2	1	sable	3	2
Delta	2	2	scarlet	2	1
deltex	2	1	scute	4	1
Dichaete	3	3	sepia	4	1
dusky	6+	3	singed	5	3
ebony	10	5	Star	2	1
eyeless	2	2	tan	3	2
fat	2	2	tetraploidy	3	1
forked	9	4	triploidy	15±	1
fringed	2	1	Truncate	8±	5
furrowed	2	2	vermilion	12±	2
fused	2	2	vestigial	6	4
garnet	5	3	white	25±	11
Haplo-IV	35±	1	yellow	15±	2
inflated	2	1			

There is also another fact that a study of the mutation process has brought to our attention. The same mutation may recur again and again. A list of these recurrent mutations of Drosophila is given above. The reappearance of the same mutant indicates that we are dealing with a specific and orderly process. Its recurrence recalls Galton's famous analogy of a polygon. Each change corresponds to a new stable position (here perhaps in a

chemical sense) of the gene. Tempting as is this comparison, we must remember that, as yet, we have almost no evidence as to the real nature of the mutation process.

The mutant types that are most often referred to, or used for genetic material, are as a rule rather extreme modifications or aberrations. This has sometimes given the impression that a mutant change involves a great departure from the original type. Darwin spoke of saltations, which are only extreme mutations, and he rejected them as materials for evolution, because, he said, such great alterations in one part of the body would be likely to throw the organism out of harmony with its environment, to which it is nicely adapted. Today, while we realize fully the truth of this statement, when applied to extreme changes producing malformations or aberrations, we have come, nevertheless, to a realization that minute changes are as characteristic of mutation as are the grosser changes. In fact, it has been shown many times that small changes that make a part a little larger or a little smaller may also be due to genes in the germ-material. Since only the differences that are due to genes are inherited, it seems to follow that evolution must have taken place through changes in the genes. It does not follow, however, that these evolutionary changes are identical with those that we see arising as mutations. It is possible that the genes of wild types have had a different origin. In fact, this view is often implied and sometimes vigorously asserted. It is important, therefore, to find out whether there is any evidence in support of such a view. De Vries' earlier formulation of his famous mutation theory might at first sight seem to suggest the creation of new genes.

The opening sentence of the mutation theory states "that the properties of the organism are made up of units, sharply distinguishable from one another. These

units are bound up in groups, and, in related species, the same units and groups of units recur. Transitions, such as seen in the outer forms of animals and plants, no more exist between the units than between the molecules of the chemist.

"Species are not continuously connected, but arise through sudden changes or steps. Each new unit added to those already present forms a step, and separates the new type as an independent species from the species from which it arises. The new species is '*presto change,*' there. It arises without visible preparation and without transitions."

It may appear from this statement that a mutation that produces a new elementary species is due to the sudden appearance or creation of a new element—a new gene. Put in another way, we witness at mutation the birth of a new gene or at least its activation. The number of active genes in the world has been increased by one.

De Vries has further elaborated his views on mutation in the concluding chapters of *The Mutation Theory* and in his later lectures on "Species and Varieties." He recognizes two processes, one the *addition* of a new element that gives rise to a new species; and the other, the *inactivation* of a gene already present. It is the second view that interests us at present, because, except for the manner of expression, it is essentially the view that is today sometimes said to be the way in which the new types in our cultures arise—through the *loss of a gene.* De Vries himself, in fact, places in this category all the commonly observed cases of loss mutations without respect to their dominance or recessiveness, implying, however, that they are recessive because their gene has become inactive. Mendelian results, he thinks, belong solely to this second category, because of the existence of contrasting pairs of genes—the active one and its inactive mate. These segre-

gate, giving the two kinds of gametes peculiar to Mendelian inheritance.

De Vries says that such a process represents a step backward in evolution. It is not progressive but degressive and produces a "retrograde variety." This interpretation is, as I have said, closely akin to a current interpretation of mutational changes as due to a loss of a gene—in principle the two ideas are the same.

FIG. 42.
Oenothera Lamarckiana (to the left), and O. gigas (to the right).
(After Castle, from Davis.)

It is not without interest, therefore, to examine the evidence that led de Vries to develop his mutation hypothesis.

De Vries found near Amsterdam, in a waste field, a colony of evening primroses, *Oenothera Lamarckiana* (Fig. 42). Amongst them were a few individuals that differed somewhat from the common forms. He brought some of these into his garden and found that they bred true for the most part. He also bred the parent form, or *Lamarckiana*. It produced, in each generation, a small number of the same new types. In all, about nine such

types were recognized at that time. These were the new mutants.

Now it has turned out that one of these types is due to doubling the number of the chromosomes. It is called gigas (Fig. 42). One is a triploid, semigigas. Several of the types are due to the presence of an extra chromosome. These are called *lata* and *semilata* forms. One at least, brevistylis, is a point-mutant, like the recessive mutants of Drosophila. It is, then, to *O. brevistylis,* and to the residue of recessive mutants, that de Vries must appeal.[1] It appears, now, highly probable that this residue (the recessive mutants) conform to the Drosophila mutant types, but their manner of reappearance in nearly every generation gives a picture entirely different from that of mutation in Drosophila and other animals and plants. A possible interpretation may be found in the presence of lethal genes closely linked with these recessive mutant genes. Only when the recessive gene is released from its near-by lethal through crossing-over is there an opportunity for it to come to expression. It has been possible in Drosophila to make up balanced lethal stocks carrying recessive genes that simulate closely Oenothera. Only when crossing-over occurs does the recessive reappear. The frequency of its appearance is dependent on the closeness of the lethal to the recessive gene.

It has been found that other species of wild Oenotheras behave in the same way as Lamarck's evening primrose, whose peculiarities in inheritance are, therefore, not due to a hybrid origin (as has been sometimes surmised), but due, in the main, to the presence of recessive genes linked to lethal factors. The appearance of the mutant types does not represent the mutation process that pro-

[1] De Vries and Stomps both thought that some of the peculiarities of O. gigas are due to other factors than chromosome number.

duced the mutant gene but rather its release from its lethal linkage.[2]

It seems, then, that the mutation process in Lamarck's primrose is probably not essentially different from familiar processes that occur in other plants and animals. In other words, there are no longer grounds for interpreting the mutation process that it shows as differing essentially from what takes place in other animals and plants, except that some of its recessive mutant genes are concealed, owing to the presence of lethal genes.

These considerations remove, I think, any necessity for assuming that a new gene is added, even when a new or progressive type of Oenothera appears. It may be that such progressive types as de Vries had in mind arise through the accidental addition of a whole chromosome to the normal set. This question will be considered in Chapter XII, but it may be said here that there is very little evidence that new species can often be produced in this way.

[2] Shull has interpreted the appearance of a number of the recessive types of *O. Lamarckiana* on the lethal-linkage hypothesis. S. H. Emerson has recently pointed out that Shull's evidence, so far published, is not entirely cogent, but it may, nevertheless, be valid. De Vries himself, in recent publications, seems not averse to accepting the lethal interpretation for certain of the oft-repeated recessive mutants that he places in the "central chromosome."