EQUINE COLOR GENETICS

Third Edition

CHAPTER 1

Introduction

THIS BOOK IS INTENDED to be a complete discussion of horse and donkey colors and includes details of their identification and genetic control. The goal is to include all color variations occurring throughout the world and fit these into a framework that is based on traditional American nomenclature as well as on the genetic phenomena controlling the color variations.

Identification and definition of horse color are important for several reasons, and each of these reasons demands a different organization and presentation of the material. Reasons for accurate horse color identification include identification of individual horses for legal, health, and registration purposes. In addition, breeders who are interested in producing or avoiding specific colors of foals find that accurate identification of colors is essential to their success.

The organizational structure of this book generally considers genetic control first, but gives a significant nod to more strictly visual identification. Some specific details of horse color are better understood from an explanation of the underlying genetic phenomena which give rise to the colors rather than from any other point of view. The importance of the genetic approach is becoming increasingly apparent as DNA-based genetic tests for several colors are now available, and these help observers to better understand the colors and the genetic basis of their production. These will be discussed where appropriate.

While genetic testing has greatly helped in some regards, it has also revealed that occasional horse colors, if classified by visual appearance alone, can have multiple genetic formulas, all leading to a similar color. This occurs with **black** horses and also with some of the light colors such as **champagne** and **pearl**, as well as **silver dapple** and **mushroom**, and more rarely with several other pairs of colors. These colors present a very real challenge in inferring genetic mechanisms from outward appearance. Fortunately, only one of the several possible genetic mechanisms for a confusing set of colors is usually common, and the few others that are possible are generally much more rare. Consequently, discussion of the colors can still proceed from the basics of the most common mechanisms, even though the more rare mechanisms that lead to similar visual results must also be considered for completeness. Note that even if some mechanisms are common and others rare, when a rare mechanism is present, it becomes the only one of importance in understanding how a specific horse or donkey will produce color in a breeding program.

Choosing a set of nomenclature for horse colors presents an interesting array of challenges. Historical approaches were necessarily based solely on visual classification, but even these older systems were detailed and technical, because they were based on a rich lore of horse-specific information. From a strict and non-equine viewpoint, nearly all horse colors could simply be described as a shade of brown or black or a mixture of those two. People with no equine background tend to lump most horses as “brown,” because to the uneducated eye they indeed are. One step beyond that approach is the traditional equine-specific nomenclature based on visual appearance. While the nomenclature varies from region to region, it has served well for centuries in identifying horses by color. It has also served as the framework under which genetic investigations were first accomplished. The genetic approach has grown rapidly in recent years, which usually simplifies—but can also complicate—nomenclature and identification of horse colors.

The presence, for some colors, of multiple genetic mechanisms causing visually similar results presents very real problems for developing a consistent nomenclature based on genetic information alone. Nomenclature can either be visually based or genetically based, but choosing either one of these as the primary organizer of nomenclature will inevitably cause problems for situations in which the other basis is a more compelling consideration. The historic, visually-based approach is the only one that is likely to succeed in field situations in which genetic details are not usually known. In contrast, the genetically-based approach can be more useful in classifying and defining the color of breeding horses when their owners are preferentially interested in producing specific colors of foals. This guide generally uses a visually based approach, but the more genetically-based approach is referred to when appropriate.

Colors are discussed in a sequence that first examines common dark colors and then builds an understanding of less common colors as a progression from the dark colors. Each section first defines and classifies a color or group of colors and then delves into the details of genetic control. Patterns of white hairs, which can be superimposed on any background color, are examined in a similar fashion after all basic colors are considered.

Donkey colors are the subject of a separate discussion following the section on horse colors. The donkey color discussion is organized in a manner similar to that of the horse color section, but is shorter. Much less is known about donkey color than horse color, and subtle details of donkey color are understood more readily when considered in the light of horse color identification and genetics. Mule colors are omitted, except for a few examples. This is because mule colors are somewhat less well understood than those of horses and donkeys, but at the same time they are generally consistent with the expected interactions of the two parent species.

Photographic illustrations are contained in a single chapter following the text chapters dealing with the various colors. This organization allows the many subtleties of each photograph to be noted as they pertain to different details from different sections of the text.

Appendices follow the text and the illustrations. Appendix 1 is a list of color names that are included in the text. It is an attempt at a reasonably complete single list of horse color names and their main distinguishing features. Appendix 2 lists the various genes affecting horse color, including both the loci and alleles, and their actions. Appendix 3 lists genotypes of the different colors so that breeders can more adequately understand them and predict the possible color outcomes from mating various colors of horses. Appendix 4 is a table outlining the various alleles present in different breeds. It can be used by breeders to develop the potential array of colors in various breeds. Appendix 5 is a large and cumbersome table that outlines the potential results of mating various parental colors. Appendix 6 includes data that have not been published and that are important to the understanding of some principles outlined in the text.

Basic Considerations of Horse Color Identification

One purpose for understanding horse color is to be able to identify horses accurately. Accurate identification of horse color is a key ingredient in understanding the genetic or biologic basis of color and is the foundation upon which genetic investigations are built. Even a casual observer soon realizes that horses have a wide variety of colors. A standardized classification is necessary to begin communicating subtle differences between some specific horse colors, and any standardized system of color nomenclature depends on observers viewing a horse’s color in the same general way. Different languages usually have distinct approaches to describing and classifying colors of horses, and these distinctions are due to cultural differences in deciding which specific characteristics of color are most important. Different classification systems each proceed logically from a few key characteristics, although these characteristics vary from system to system. The approach of each language has merit, even though the internal logic is distinct for each. Languages and cultures tend to vary enough that a concise one-to-one correlation of color names is usually impossible between languages, because some details are simply lacking in some languages.

An ideal system of horse color nomenclature would be one wherein each unique color name corresponds to a specific genotype and each specific genotype results in a unique color name. This one-to-one correspondence between genotypes and names is lacking in all systems of nomenclature, sometimes for biological reasons, but more frequently for cultural and historical reasons. Although a tight one-to-one correspondence of terminology and genetic foundation is ideal, it is important to acknowledge that all nomenclature systems have a cultural and historic backdrop and that each has merit for specific details. For example, the one color group **chestnut** is seen as three different colors (**alazán**, **ruano**, and **tostado**) by some Spanish-speaking traditions.

Attempts to force a genetically-based nomenclature onto descriptions of horse color are becoming increasingly common. Unfortunately, these attempts are likely to fail the test of being useful systems for field identification, even though they may have great utility for horse breeders interested in producing specific colors. The failure of newer, contrived, systems is nearly assured because older and time-tested systems of nomenclature based on visual appearance have been successfully used for millennia. Also, some single colors result from distinct and different genetic mechanisms, and therefore a one-to-one correspondence of genotype and color is impossible without genetic testing. Combinations of some of the dilution mechanisms are notoriously consistent in producing beige horses with brown manes, tails, and lower legs, and yet each of these horses comes to its similar color through a different genetic combination. These pale horses, though all are a similar color, will each produce a very different array of colors in their foals.

The similar visual results of multiple genetic mechanisms are doubly confusing if nomenclature separates them and demands documentation of genes and alleles for each horse before it can be classified by color. A strategy for compensating for the lack of a one-to-one correspondence between nomenclature and genetics is to note the multiple genotypes included under a color name wherever possible. Likewise, the reverse problem of a single genotype giving rise to colors that are assigned different color names can be noted. These confusing situations are fortunately rare, so that a general trend toward one-to-one correspondence of color name to genotype is indeed the case. Those cases in which multiple mechanisms exist usually consist of one very common mechanism and one or two additional, but very rare, ones.

A few concepts form the sound foundation from which horse color can be understood, regardless of the system of nomenclature. The first important concept to understand in horse color identification is that background colors of horses occur independently of any white markings horses may have. White hairs occur as a result of hair lacking pigment granules, so white patches, markings, or individual white hairs result from absence of color rather than being a true color in themselves.

An incorrect belief, held by many people, is that various colors are superimposed on a white horse in much the same way that an artist applies paint to a white canvas. Any white areas, they believe, simply did not receive color. Thus, this incorrect idea holds that horses are basically white. However, the truth is just the opposite; white is superimposed on and covers up areas genetically destined to be specific colors. Moreover, the genetic actions determining the color of the colored areas, as opposed to those determining the extent and location of the white areas, generally operate independently of each other.

It is very important to understand that white is superimposed over some color that would otherwise have been present. All horses have the genetic capability to produce pigment over all the body. This capability has been changed on some horses (or on portions of some horses) by a superimposed genetic directive to impede the development of color, leaving white hairs or areas. The basic color of a horse must therefore be considered by first ignoring any white areas. Horses that are entirely white or nearly so will, of course, make this approach impossible. However, the tactic of first ignoring white works well for most horses and is essential in deciding the basic color of a horse. For this reason patterns of white are discussed in the chapters following those on basic colors because the two categories (color and patterns of white) are so distinct genetically and biologically.

Another important concept is the definition of the "points" of a horse. In horse color terminology the points are the mane, tail, lower legs, and ear rims. The importance of the concept of the points is that their color usually determines the name given to the overall color combination on a horse. Specific combinations of point color and body color determine most horse color names.

The two main groups of horse colors are those with black points and those with nonblack points. Nonblack points are usually red or cream, but occasionally are a brown color. The division of points into black and nonblack is important for identification and also has important genetic implications. Specific combinations of point color with body color yield the final color name, so once point color is appreciated it becomes fairly easy to identify most horse colors.

Black and nonblack points are usually easy to distinguish from one another. In some instances black manes and tails become faded or sunburned to brown, and in these cases the lower leg is the most accurate indicator of point color. In most horses with black points the black carries to the hoof and involves at least the pastern. In most horses with nonblack points the pastern and coronary region are lighter than the remainder of the lower leg, so this region is very useful in deciding whether a horse has black or nonblack points. Distinguishing between the two groups of point color is usually simple because horses with confusing point color are rare.

Two situations in which point color can be confusing are foals and horses with extensive white markings. Foals of all colors frequently have very pale points, even on those colors that have black points as adults. Whereas experienced observers can usually predict adult coat color from characteristics of the foal coat, exceptions are numerous and frequent enough that all observers should be cautious in predicting adult color from foal coat color, especially in breeds with wide color variation.

Horses with extensive white marks can have their point color completely masked by the white marks. In these cases mane and tail color become the most important indicator of point color. It is essentially impossible to accurately determine point color on some horses with extensive white marks.

Various combinations of point colors and body colors are given different names in different geographic regions, and no single system or language is complete for naming the details of all of these combinations. The approach taken in this guide is consistent with the usual approach in the western United States of America. The westerners in the United States developed a fairly detailed vocabulary for describing horse color. This vocabulary functions well for nearly all color variations possible on horses. A few rare colors or combinations have no names in English. In such cases other cultures or languages have been consulted for names and concepts that will help in understanding these rare colors and how they occur. While other languages and cultures have been considered, the final nomenclature is usually an English equivalent so that English speakers can more readily understand and use the concepts adopted from these sources.

A detail that can sometimes lead to confusion is that horses can vary in color from season to season or year to year. Horses are generally darkest when they shed their thick winter coats in the spring. Sun, wind, and rain can then act to bleach the color, although some horses remain unaffected by such weathering. Horses also can change shade of color due to their state of nutrition, condition, and general health. Healthy, well-fed, and well-conditioned horses are usually darker than are those less fortunate horses lacking the same benefits.

An additional detail that becomes a problem confronting an observer of horse color is the inescapable fact that every color varies over a range from light to dark. It is therefore always possible to find some individual horses that are at the boundary of two defined colors. This is simply a consequence of the complexity of the genetic control of horse color, coupled with the uncertainties and inconsistencies of the environment. A thorough understanding of the genetic control of horse color can be helpful in such instances because an observer is then at least able to understand how the color arose, and this can help answer the question of color terminology if only through the backdoor. The overall process of correctly identifying horse color begins with the descriptive stage. Descriptive knowledge helps in the understanding and appreciation of the biologic (genetic) control of color. Finally, knowledge of genetic control circles back to enhance the appreciation of descriptive categories and subtleties.

Horse color is generally believed by most breeders to be only a cosmetic detail. But many horse owners, and indeed entire horse-using cultures, have long attributed specific characteristics to horses of specific colors. Most such beliefs are generally dismissed as fiction, but a kernel of truth may well lie behind a few of them. A small collection of European research is beginning to verify that horses of specific colors tend to react somewhat predictably in certain situations and that these reactions vary from color to color. A general trend seems to be that horses of darker colors are livelier than lighter ones, but the breeds in which this was determined were not noted, so the range of colors is likewise uncertain. While any behavioral connections to horse color are far from proven, these tidbits of folklore will be noted as the different colors are discussed. Even though relationships of behavior and color are speculative, they are an interesting part of the art of horse breeding and horse keeping. The interaction of color and behavior is treated briefly in *Domestication: The Decline of Environmental Awareness*, listed in the bibliography.

Basic Principles of Genetics

A thorough understanding of the genetic control of horse color takes study and hard work. The reward is an enhanced appreciation of horses and their beauty and more accurate descriptions of horses for registration purposes. An understanding of genetics is almost essential for breeders interested in producing specific colors of foals. A brief overview of some principles of genetics as well as some definitions of genetic terms is a good starting point for this endeavor.

A horse’s color results from the interaction of at least thirteen generally independent processes (or factors). Most of these are specific genetic loci; others have not yet been characterized. Interaction of so many factors unfortunately means that the control of color is inherently complicated; it cannot be made completely simple. The genetic basis for most of the thirteen processes controlling color has been documented by a variety of scientific studies, resulting in a fairly complete understanding of them. However, the theoretical basis for some of the processes is currently only an educated guess.

The interaction of all of the factors results in the many different shades and types of horse colors. For most colors, each specific combination of interacting components results in a unique color, although a few colors are exceptions to this rule. The genetic basis of the colors therefore neatly explains most of the colors by accounting for the complex interactions that cause them. These interactions can be understood best if the basic factors are taken one at a time.

In this way the number of complex interactions can be broken down into fewer key components, and the colors can be understood sequentially by adding the effects of each of the processes in turn.

Genes are responsible for all biochemical processes that occur in living organisms. Genes are made of deoxyribonucleic acid (DNA), which functions as a long string of repetitive components that form a code. In horses, as in all mammals, genes occur on chromosomes.

While modern techniques are revealing that chromosomal organization is very complicated, they can still be loosely thought of as strings of genes to facilitate understanding the basics of their function as genetic units passing from generation to generation. Chromosomes occur in pairs; an individual gets one of the pair from the sire and the other from the dam. When an individual reproduces, it contributes a random half of its chromosomes (one of each pair) to its offspring. The other half of the resulting offspring's genetic makeup comes from the mate. This halving of genetic material from parents and pairing in offspring is the mechanism by which the genetic code works its way through generations and populations, and is also the source of variation from parents to offspring as the combinations are reshuffled in each generation.

It is essential to understand the concept of halving and subsequent pairing at each generational step to appreciate the impact of genetics on horse color. The recombination of pairs at each generation is the basis of how genetics operates. The components of the pairs are constrained by the specific variants in the parents, and only those parental variants will be available for contribution to the offspring. Recombining of genes generation to generation is frequently called "segregation" because the genes can appear in different combinations at each generational step.

Each gene occupies a specific site on a specific chromosome. This site is called a locus (plural, loci), and frequently genes are described by their locus names. Locus simply means an address for a gene: it is a specific physical place that a gene occupies. Both members of a pair of chromosomes in a horse have identical loci, all lined up in the same sequence. The only exceptions are a few, generally pathologic, situations. Usually the term locus, even though singular, applies to a specific site on both chromosomes of an individual animal. For example, the *Agouti* locus in a horse implies the specific genetic site on two chromosomes (one from the sire, and one from the dam), each coding for the same piece of genetic information. Specifically, the *Agouti* locus is found at a specific site on horse chromosome 22. It is found at that same site on chromosome 22 inherited from the sire as well as the chromosome 22 inherited from the dam, and indeed is at that same site in all horses.

When a gene occurs in more than one form, the different forms are called alleles. The alleles of a gene all occur at the same locus, although each chromosome is limited to having only one allele. The result is that each horse has, at most, a total of two different alleles at any locus because it has only two of each chromosome. The wide variety of horse colors results from individual horses differing from one another in the specific allelic combinations they have at various loci controlling the different components of color. These numerous allelic combinations cause the variations that humans perceive as the range of colors in horses. The specific combination of alleles, or genetic makeup of a horse, is called its genotype. The external appearance or physical makeup is called the phenotype. The phenotype may or may not completely reveal the underlying genotype.

The condition of having two identical alleles at a locus (one on each chromosome) is called "homozygous." When the alleles are different, the situation is called "heterozygous." This terminology (homozygous/heterozygous at a locus) reflects back to the concept of "locus" as encompassing a specific site on both of two chromosomes that code for the same gene.

Alleles at a genetic locus interact in a variety of ways. Some alleles are not expressed phenotypically unless both doses of the gene in an individual are the same (homozygous). These are recessive alleles (or genes, the two terms are sometimes used interchangeably). Dominant alleles, in contrast, are expressed identically whether in one dose (heterozygous) or two doses (homozygous). The main concept is that a dominant allele masks the phenotypic expression of a recessive allele when the two are paired in the heterozygous condition. As a result, colors associated with recessive alleles can appear to pop up out of nowhere because they can be carried along, unexpressed phenotypically, through several generations, while paired with dominant alleles. Recessive alleles are perceived as surprises when they become expressed by virtue of being paired in the homozygous offspring of two individuals that carry them. In this case, the carrier parents do not show the effect of these alleles because they are being masked by dominant alleles. Dominant alleles cannot be carried along in a hidden state in this manner. If a dominant allele is present, it is expressed phenotypically. As a result, dominant alleles, if present, show up in each generation and therefore are not the source of surprises except very, very rarely, such as in the case of a spontaneous mutation. Mating of recessive to recessive can yield no surprises because nothing is hidden, and the phenotype therefore betrays the genotype completely, or nearly so.

It is important to understand that the character of an allele as dominant or recessive is inherent in the character of the allele itself. This does not change over time, nor does it change in various situations. Many people are under the mistaken impression that dominant alleles are necessarily common and that recessive alleles are necessarily rare. The issue of allele frequency is totally separate from the issue of dominance and recessiveness. Some recessive alleles, such as *chestnut*, are indeed common to the point of being uniform throughout some breeds of horses such as the Suffolk. The uniformity of the *chestnut* allele in the Suffolk in no way changes its character as a recessive allele, so that crosses of Suffolks to black Percherons result in few if any chestnut foals, because the black points of the Percheron will dominate the *chestnut* allele of the Suffolks. Likewise, some dominant alleles, such as *white*, are incredibly rare or nonexistent in most breeds and yet are routinely passed as dominant alleles in those few families in which they occur.

Some alleles are described as incompletely dominant, which means that two, one, or no doses each results in a separate appearance. Each situation can be detected phenotypically by examining external appearance. Incompletely dominant systems are the easiest to understand, because no surprises can result as occurs with hidden recessive alleles. With incompletely dominant alleles, the two different homozygous genotypes, as well as the heterozygous genotype, each have a distinct phenotypic appearance.

Another interaction of genes is called epistasis. This refers to the ability of specific allelic combinations at some loci to mask the expression of alleles at another locus. Epistasis is another example of the complexity of genetic interactions. It is similar to the relationships of dominant and recessive alleles, but concerns two or more loci instead of only one. The gene that is masked by an epistatic gene (or allelic combination) is referred to as being hypostatic, while the gene or combination causing the masking is called epistatic. Hypostatic genes can pop up as surprises, much as do recessive genes when masked by dominant ones. Specific examples in the discussion of the colors will illustrate this phenomenon and will help in the understanding of what can be a subtle and confusing concept.

Genetic loci can be considered as separate little biochemical factories. Each locus controls some unique aspect of the color that is finally produced and seen. It is convenient to consider the control exercised by each locus as a switching mechanism. At most loci the choice is either “situation A” or “situation B.” Thinking about the loci as switches helps in understanding that each locus presents a choice and the choice at each locus will affect the resulting color. If each locus is considered to make a separate component of the final appearance, it is easier to understand how color arises as the final result of specific combinations of choices. By understanding the components it is possible to appreciate the interactions that lead to the color that is present on the horse. Because each locus has only two (or a few) choices, the components are fairly easy to understand once they are identified and appreciated as such. The concept of each locus doing a separate job is the key to understanding the genetic basis of horse color. By viewing genetics in this way it is possible to appreciate how the various colors can be built in successive steps from the various component parts.

Genetic nomenclature is subject to a number of conventions, and these are variable in much of the literature. A standard format is used throughout this guide, and follows the guidelines of the Committee on Genetic Nomenclature of Sheep and Goats, which has been expanded to now include other domesticated animals. Names of loci have an initial capital letter to distinguish them from names of alleles, which are all in lowercase letters. Both loci and alleles are in italic type. *Dun* is a locus, *black* is an allele. The symbols for loci are abbreviations of the names and are in italics, with an initial capital letter. Allele symbols are added to locus symbols as superscripts to separate them from the locus symbol. The symbol "+" is used to denote the probable wild-type allele at a locus.

For example, Dn^+ is the *wild type* allele at the *Dun* locus. The wild type is inferred from the probable original color of horses before their domestication. Symbols for alleles other than *wild type* are standardized so that dominant alleles have an initial capital letter, while those for recessive alleles have a lowercase letter. This convention is used even though names of both dominant and recessive alleles, when spelled out and not referred to by symbols, have an initial lowercase letter.

Another convention is the abbreviation of genotypes by using dashes to fill in behind dominant alleles when the second of the pair is unknown or unimportant. For example, A^A- (*bay* at the *Agouti* locus) can be used for A^AA^A and A^AA^a, which both appear the same phenotypically. A^aA^a (a genotype with two *black* alleles at the *Agouti* locus) has no abbreviation, because a recessive genotype masks nothing, although sometimes A^a will be used as a phenotypic abbreviation for A^aA^a.

A further problem in nomenclature is becoming increasingly common as the biochemistry and molecular mechanisms of the loci become established. It is now common for the older symbols to not match the loci documented by results of molecular investigations. Most of the newer locus names and symbols are based on mouse nomenclature, because the genetics of mice has been so much more extensively characterized than that of any other species. Where possible the molecular loci are noted, while the older symbols are still retained because long use has made these widely accepted and understood. To change them to match the molecular aspects would increase confusion, rather than reduce it.

Another convention used throughout this guide is the printing of names of horse colors in bold type. This reduces confusion between a discussion of a color in general and a specific name for a horse color. Black, for example, is a general name for a color in nature, while **black** is specifically the color of a **black** horse. Other peculiarities of eye color and hair are also printed in bold type because these also have specific connotations when used concerning horses.

Pigments in Horses

A fundamental principle to understand about horse color is that color in horses is due to the presence of pigments in the hair. Two major pigments account for all colors of mammals (including horses). One of these is eumelanin (YOO-mel-a-nin), which is responsible for black or slate blue. In a very, very few horses eumelanin is brown (flat, chocolate brown) rather than black, but these horses are rare. This chocolate brown type is the color that is common in retriever or spaniel dogs. The switch between black and brown eumelanin is an “either/or” phenomenon for the whole horse: a horse can form either black or brown, but not both. This is an important detail, even though the colors based on brown are so rare.

The other pigment is pheomelanin (FEE-oh-mel-a-nin), which produces colors ranging from reddish brown or tan to yellow. Pheomelanin can vary in shade on a single horse, and on many individual horses pheomelanic areas do indeed vary from dark to light. Most horses have both pheomelanic and eumelanic areas on them and are therefore combinations of black and red or yellow pigmented areas. Dark pheomelanin sometimes can resemble brown eumelanin and is much more common than eumelanin as a source of any brown areas on horses. Pheomelanin usually retains at least some of its reddish color, even when very dark, and this reddish tinge helps to distinguish pheomelanic areas from eumelanic areas.

White hairs result from a lack of pigment granules, and these are essentially hairs without color. Skin that lacks pigment granules is characteristically pink, and it gets its pink tone from the presence of blood in small, superficial blood vessels.

Pigment Cell Function

Color in horses is possible because pigment cells, called melanocytes, act to put pigment granules into cells that become hair and skin. The presence and function of these cells determines the amount, type, and character of pigmentation.

Melanocytes migrate to the skin in embryonic life. They originate along the neural crest, which also gives rise to the spinal cord and brain. The importance of this detail is that the pigmentary system and the nervous system are closely allied in embryologic life, and some specific genes affect both of these instead of only one or the other.

Melanocytes can produce either pheomelanin or eumelanin. A receptor on the surface of melanocytes determines which pigment is formed This receptor can be activated by melanocyte-stimulating hormone, which is elaborated by the pituitary gland at the base of the brain. In the absence of activation, cells form pheomelanin. When the receptor is activated, the result is eumelanin formation.

The switch between eumelanin and pheomelanin production can be influenced at several different steps. One switch is the presence or absence of melanocyte-stimulating hormone, which activates the receptor. This is a fairly rare switching mechanism and is unimportant in horse color because melanocyte-stimulating hormone is fairly constantly available to all cells of horses.

A second switch is at the level of surface receptors. These are coded by the *Extension* locus as well as a few other loci. Some mutations, such as *dominant black*, produce a receptor stuck in the "on" position in many species. The result is an entirely eumelanic phenotype. In this situation the receptor is always activated, even in the absence of melanocyte-stimulating hormone. Other mutations, such as *chestnut*, result in a totally inactive receptor that is incapable of responding to melanocyte-stimulating hormone and therefore results in a completely pheomelanic phenotype in most cases.

A third way to affect the switch is to block the surface receptor externally. This leads to an inability of the receptor to be activated even though the receptor is normal and melanocyte-stimulating hormone is present. This mechanism is typical of the *Agouti* locus and results in pheomelanin in those areas of the body that express the agouti protein (blocked receptor) and eumelanin in others where this protein is lacking (unblocked receptor). The regional distribution of the agouti protein is under genetic control.

The internal workings of the melanocyte are as important as the surface receptor in determining the final production of pigment. The formation of eumelanin and pheomelanin involves several steps, some of which are common to both pigments and some of which are unique to one pigment or the other. This is important because some mutations affect the production of only one of the two pigments, while others affect the production and character of both. The loci controlling the internal packaging and production of pigment in horses are increasingly being characterized at the molecular level. As a result, past uncertainty concerning homologous loci (those with identical function) in other species is slowly being resolved. This contributes to a deeper understanding of the specific mechanisms leading to the various colors of horses.

The pigments are formed in small packages called melanosomes. These can be moved from the melanocyte to surrounding hair and skin cells. The packaging and distribution of melanosomes is subject to changes, and these can result in different visual appearances of colors that are caused by identical pigments. These changes are under genetic control at yet other loci distinct from those mentioned previously.

In general, the consequences of mutations in the external or surface environment of the melanocyte result in changes in the determination of eumelanin versus pheomelanin (the *Extension* and *Agouti* loci). Changes in the internal machinery of the melanocyte usually result in changes in the amount of pigment produced or how it is packaged. The consequences of internal changes usually determine the degree of dilution of pigment rather than changes in the specific pigment produced (loci controlling *Dun, MATP [Cream and Pearl], Champagne, PMEL17 [Silver Dapple],* and *Mushroom*). The difference between the two sites (surface versus internal) is one of “which” (surface) versus “how much” (internal).

White spotting is controlled at yet other loci that affect the migration, survival, or function of melanocytes. A few consistent loci appear to cause white spotting in several species. One of these is the receptor for endothelin B, which is affected by the *frame* mutation. Other good candidates for white-spotting mutations include the mast cell growth factor locus (the *KIT* locus). This locus appears to be affected by several mutations and is thought to be the locus responsible for several different white spotting patterns such as *roan, sabino 1*, *dominant white,* and possibly *splashed white*, or very close to the affected site (*tobiano*). The homologies of white-spotting alleles with those of other species are still not fully documented in horses.