Available online at www.sciencedirect.com
ScienceDirect
Livestock Science 117 (2008) 109–129
LIVESTOCK SCIENCE
www.elsevier.com/locate/livsci

Review article

Coat colour inheritance in horses

A.K. Thiruvenkadan *, N. Kandasamy, S. Panneerselvam

Department of Animal Genetics and Breeding, Veterinary College and Research Institute, Namakkal-637 002, Tamil Nadu, India

Received 10 September 2007; received in revised form 12 May 2008; accepted 15 May 2008

Abstract

The colours of the horses have long been a subject of interest to owners and breeders of horses as well as to scientists. Though, the colour of horses has little to do with its performance, it is a primary means of identification and also the first indicator of questionable parentage. Probably the ancestral colour of the horse was a black-based pattern that provided camouflage protection against predators. Horse colours are mostly controlled by genes at 12 different loci. The three basic colours of horses are black, bay and chestnut. The genetic control of the basic colours of horses resides at two genetic loci, namely Extension (E) and Agouti (A) loci. Among the basic colours bay is dominant to black and both are epistatic to chestnut. Dilution of basic colours of horses as a result of four colour dilution genes such as cream dilution, dun, silver dapple and champagne resulted in extensive array of possible colours of horses. The most widespread and familiar of the horse colour dilution gene is the one that produces the golden body colour and are called as palomino or buckskin based on the colour of the points. The grey coat colour is due to the presence of dominant gene (G) at the grey locus. Grey is epistatic to all coat colour genes except white and a grey horse must have at least one grey parent. Roan is due to a dominant gene (Rn) at roan locus and this combines with any base colour to produce the various shades of roan pattern. White coat is due to a single dominant gene (W) and it is epistatic to the genes controlling all other colours. White marking in the face and legs are due to genetic and non-genetic factors. Several genes are involved in producing white markings. During recent years, comparative genomics and whole genome scanning have been used to develop DNA tests for different variety of horse colours. Molecular genetic studies on coat colour in horses helped in identification of the genes and mutation responsible for coat colour variants. In future, this will be applied to breeding programmes to reduce the incidence of diseases and to increase the efficiency of race horse population.

Keywords: Horse; Coat colour; Melanogenesis; Genetic control; Molecular genetics

Contents

* Corresponding author. Tel.: +91 4272341645.
E-mail addresses: drthirusiva@yahoo.com, drthirusiva@rediffmail.com (A.K. Thiruvenkadan).

1871-1413/$ - see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.livsci.2008.05.008

1. Introduction

Coat colour in general has intrigued scientists all over the world for centuries. Such an interest could be explained by its phenotypic characteristics being easily recognizable, making it simple to follow the inheritance from generations to generations. Therefore, coat colour has become a model phenotype for studying gene action and gene interactions. The colours of the horses have long been a subject of interest to owners and breeders of horses as well as to scientists. Much information on them is found in the studbooks of particular breeds. Attempts to use this information in framing explanations of the observed results of mating have been made repeatedly since the rise of genetics. Though, the colour of horses has little to do with its performance (Dring *et al*., 1981; Bowling, 1996; Sponenberg, 1996; Stachurska *et al*., 2006), it is a primary means of identification and also the first indicator of questionable parentage. Probably the ancestral colour of the horse was a black-based pattern that provided camouflage protection against predators. The horse has clearly evolved into an animal with a wide range of colours. No colour in horses appears to be confined to a single breed, suggesting that the mutations producing the colour variants occurred early in the domestication time frame, before the development of modern breeds (Bowling, 1996). Dark horse colours are generally the most common colours in any breed, and are usually referred to as dark or hard colours. Black, bay and chestnut are the basic colours of horses and from which all other horse colours are built by various modifications (Lauvergne *et al.* 1991; Sponenberg, 1996). A large number of literature have been published on coat colour inheritance in horses by different authors and compilation of the same has been made in books (Bowling, 1996; Sponenberg, 1996; Bowling, 2000). The major objective of this review is to give a comprehensive picture on coat colour inheritance of horses by incorporating recent molecular genetic studies.

2. Melanogenesis in mammals

Melanogenesis refers to the biosynthesis of melanin pigment in specialized pigment cells called melanocytes. Melanins reside in cellular organelles called melanosomes, which are produced by melanocytes. Mammalian coat colour is almost entirely dependent on the presence or absence of melanin in the skin and hair; eye colour is mainly determined by intraocular melanin (Searle, 1968; Moellmann *et al*., 1988; Sponenberg, 1997).

2.1. Migration of melanocytes

In order to comprehend the full complexity of genetic control of pigmentation, it is necessary to understand the process of formation of melanocytes from the neural crest. It is an early embryonic structure, which lies along each side of the neural tube. Neural crest cells are the primary source of several vertebrate structures and help in the formation of many others. Thus most of the visceral skeleton, the head and trunck mesenchyme, the cephalic, spinal, sympathetic and visceral ganglia, the melanocytes and the sheath cells of Schwann are wholly or partly derived from neural crest material (Horstadius, 1950). From the first group of neural crest cells, the embryonic melanoblasts arise. They are small and round or ovoid, later becoming stellate and finally dendritic when they mature. During embryogenesis the pigment cells (melanocytes) migrate to specific sites on either side of the body as well as the backline. There are three such sites on the head (near the eye, ear, and top of the head), and six sites along each side of the body, and several along the tail. A few pigment cells migrate to each of these sites, there they proliferate and migrate outwards, joining up to form larger patches, spreading down the legs and down the head until they meet up under the chin, and down the body until they meet up on the belly (Cattanach, 1999). The pigment cells are very numerous at the dermo-epidermal junction. From there they can migrate into the hair follicles or remain in the epidermis. The two functional forms of melanocytes are one with melanin and other without melanin. Both are normally present in hair follicle, though only amelanotic form is present in albinos, each can change into the other (Staricco, 1963). Once the pigment cells have finished migrating they reside in the bulb of hair follicles. There they synthesize melanin pigment, which are incorporated into the growing hair.

2.2. Melanin synthesis inside the melanocytes

Melanin pigment is synthesized in little vesicles inside the melanocytes called melanosomes. There are two types of melanosome namely eumelanosomes and phaeomelanosomes. Melanosomes produce pigments inside the melanocyte. The melanosomes migrate from the middle to the edge of the melanocyte with the help of microtubules. At the outer edge of the cell, melanosomes release their pigment by a process of exocytosis, which transfers the melanosomes from the dendritic processes of the melanocytes into the epidermal cells, which are then incorporated into the surrounding keratinocytes and the shaft of the growing hair (Searle, 1968; Moellmann *et al*., 1988; Sponenberg, 1997).

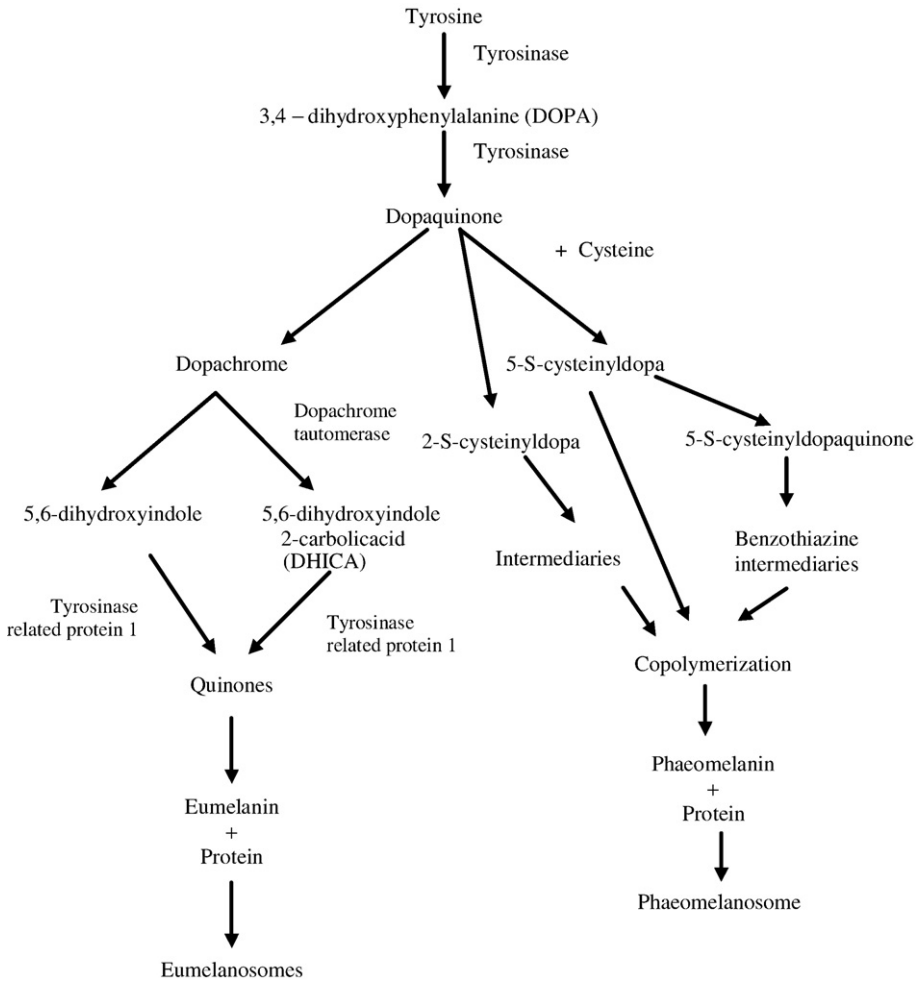

Fig. 1. Melanin synthesis-biochemical pathway (Adopted from Searle, 1968; Robins, 1991).

2.2.1. Biochemistry of melanin synthesis

Both eumelanin and phaeomelanin pigments are synthesized from the amino acid tyrosine with the help of an enzyme tyrosinase. The enzyme tyrosinase converts tyrosine to dopaquinone (Fig. 1). To make eumelanin, dopaquinone is converted to dopachrome. Dopachrome can take two pathways to eumelanin synthesis. In the first pathway, dopachrome is converted into 5,6 dihydroxyindole which is brown and then into complex quinones by the enzyme tyrosinase related protein 1 (TYRP 1). In the second pathway it is converted into 5,6 dihydroxyindole 2-carbolic acid (DHICA) by dopachrome tautomerase and from there to complex quinones by TYRP 1 again. Complex quinones are then polymerized into eumelanin. For phaeomelanin synthesis, dopaquinone is converted to 2-*S*-cysteinyldopa (minor product) and 5-*S*-cysteinyldopa (major product), which then through different intermediate steps produces phaeomelanin (Searle, 1968; Jackson, 1994; Robins, 1991).

2.2.2. Difference between eumelanosomes and phaeomelanosomes

There are ultrastructural differences between eumelanosomes and phaeomelanosomes. The two types are identical in stage 1 (i.e., spherical membrane bounded vesicles) but subsequently eumelanosomes become ellipsoidal in shape and show an internal lamellar structure. Whereas phaeomelanosomes remain spherical shape and do not develop lamellae (Robins, 1991). There is also difference in contents of the melanosomes. The eumelanosomes produce a melanin pigment called eumelanin that lacks sulphur and ranges in colour from dark brown to black. It is an insoluble brown indole-quinone polymer of high molecular weight. The major isomer of eumelanin is dopaquinone, whereas phaeomelanosomes produce a

melanin pigment called phaeomelanin, which is rich in sulphur and range in colour from red to yellow. It is soluble in dilute alkali and is slightly fluorescent in UV light of wavelength 366 nm. The major isomer of phaeomelanin is 5-*S*-cystinyldopa (Searle, 1968). While there is homogenous accumulation of eumelanin in eumelanosomes, phaeomelanin is deposited in a discrete manner in phaeomelanosomes. The biochemistry of pigment production in horse is by and large homologous to that of other species (Woolf and Swafford, 1988). Skin that lacks pigment granules is characteristically pink, and it gets pink tone from the presence of blood in small, superficial blood vessels (Sponenberg, 1996).

2.3. Genetic basis of pigmentation

The colour of mammalian coat depends on a large number of variable factors, themselves interdependent. First, there are the melanin granules, their composition, numbers, shape and arrangements of which may all influence the final result. These in turn depend on the presence and properties of the melanocytes and of the different kinds of hair. The cellular environment is also an important factor in determining the type of pigment produced by the melanocyte. In addition, presence of the melanocyte depends on its successful migration and on the normal development of the neural crest from which it stems. Thus the desired end-result depends on the proper functioning of a hierarchy of genes becoming active at different times and in different places or some times acting throughout the organism at the same time. In general the mammalian coat colour and eye colour pattern may be changed by genes acting on the following structures (Searle, 1968).

2.3.1. Neural crest

There are many mutations that may affect the migration of the cells from the neural crest. The hooded allele in the rat delays the migration of melanocytes from the neural crest. Consequently, the areas furthest from the dorsal midline i.e., feet, chest, belly do not have melanocytes and those areas produce depigmented white hair. Very many different mutants that affect migration of the cells from neural crest region cause lethal white-spotting condition. These mutations affect normal melanocytic and enteric neural crest cell differentiation, proliferation and migration during development (Searle, 1968). This leads to depigmentation and also lack of neural connections to the colon. Hence bowel cannot be evacuated. This condition is called as megacolon and it is fatal. This condition is noticed in mice and some other mammalian species.

2.3.2. Migrating melanoblasts

Genes acting directly on the melanoblasts after they have left the neural crest might prevent them completing differentiation, thus leading to a white phenotype or might possibly just reduce their final population. This could have a general diluting effect. Most of the diluting genes are known to involve the later stages of melanogenesis.

2.3.3. Cellular environment of the melanoblast

2.3.3.1. Melanocyte morphology. A morphological change in the melanocyte may mean that it does not fulfill its function of synthesing and secreting pigment granule in the normal manner. Genes at two loci in the mouse, dilute (d) and leaden (ln), have this sort of effect when homozygous. The epidermal melanocytes of these mutants are nucleopetal in type having fewer and finer dendritic processes and the melanin granules are mainly confined to the central part of the cell around the nucleus, whereas, normal nucleofugal melanocytes have numerous and thicker dendritic processes and the melanin granules are present in these processes as well as around the nucleus (Markert and Silvers, 1956). As a result of nucleopetal type of melanocytes in mutants, the melanin granules secreted into hair are arranged in clumps rather than being evenly spread, leading to lightening of colour even though there is little change in the actual number of pigment granules (Russell, 1948).

2.3.3.2. Protein structure of the pigment granules. Mammalian pigment granules consist of melanin attached to protein; if the nature of the protein is changed then this might be reflected in the shape of the granule, which could in turn lead to an alteration in coat colour. An example is pink-eye dilution (P) in mice, which causes eumelanin granules to have an irregular shred-like shape and be somewhat smaller than normal. They also tend to form large flocculent clumps, which, with the reduced amount of pigment, is the reason for the fur-colour dilution. Almost all pigment is removed from the eye so that it is pink (Moyer, 1960).

2.3.3.3. Stages in the synthesis of melanin. The various biochemical steps in the synthesis of the different forms of melanin are gene-controlled. Thus mutation to new alleles at any one of a number of loci may reduce or abolish melanin production or cause a switch from production of one type to production of another.

2.3.4. Hair formation

If hair formation and resultant hair structures are defective there may as well be an effect also on

pigmentation because i) pigment granules may be unable to enter the hair or ii) their distribution within the hair may be abnormal, even if they can enter it.

2.4. Allelomorphic series in mammals

Most of the allelomorphic systems related to coat colour in mammals have been recognized. The allelomorphic systems identified in mammals are not only phenotypicaly alike but are also having similar dominance relationships to each other and apparently have the same functional basis. This indicated that the loci concerned with different coat variations among mammals are homologous (Searle, 1968). The different allelomorphic systems identified in mammalian species and their main characteristics are as follows:

2.4.1. Extension series (E)

The alleles at the extension locus either extend or diminish the amount of eumelanin in the coat, with an opposite effect on the amount of phaeomelanin. In horses, the dominant allele 'E' extends the amount of eumelanin and diminishes the amount of phaeomelanin in the coat and the allele 'e' has an opposite effect.

Melanocytes are capable of forming both eumelanin and phaeomelanin, although they usually produce one or the other at any one time. The dedication of melanocytes for eumelanin production depends on the presence of α-melanocyte-stimulating hormone (α-MSH), which is a pituitary hormone (Jackson, 1994). Melanocytes have surface receptors that bind this hormone. When α-MSH binds to the surface receptors, the result is a cascade of events that activates adenylate cyclase. This activation in turn stimulates the melanocytes to produce eumelanin. In the absence of this signal, which is dependent on α-MSH as well as the surface receptors, melanocytes produce phaeomelanin. The switch between eumelanogenesis and phaeomelanogenesis depends on the function of receptors to α-MSH.

2.4.2. Agouti series (A)

The agouti locus is concerned with the regional distribution of eumelanin and phaeomelanin pigment in the coat. Hairs in the wild type agouti coat are characterised by a terminal or sub-terminal band of yellow due to phaeomelanin pigment granules, the rest of the hair showing the black or brown pigment granules. This pattern is of particular interest because it shows that the shift from one type of pigment to other can take place within a single hair.

The agouti locus is responsible for the formation of a protein that acts to nullify the action of α-MSH on melanocytes (Jackson, 1994). In regions in which this protein is present the melanocytes fail to respond to α-MSH and therefore form phaeomelanin and not eumelanin. Melanocytes in regions lacking this protein have full capability for stimulation by α-MSH and therefore form eumelanin. In regions with a pulsatile formation of the agouti protein, the result is banded hairs. The agouti locus is very widely distributed among mammals. In horses the agouti pattern is not present; however the alleles in the agouti locus produce either bay or black colour.

2.4.3. Albino series (C)

The albino series of alleles control the intensity of hair, eye and skin pigmentation. As one goes down the scale from the fully dominant (usually wild type allele, C) to fully recessive albino allele 'c', the amount of pigmentation is reduced step by step. In the final step albinism occurs. In albino types there is complete lack of melanin pigmentation, so that hair is white and eyes and skin are pink. This albino condition has been found widely in mammals. The albino locus codes for the tyrosinase enzyme that is essential for melanogenesis. Recessive alleles at the locus are responsible for the production of abnormal forms of tyrosinase that have either reduced or nearly completely absent activity. As a result, melanocytes are present, but are incapable of melanogenesis.

2.4.4. Dilute series (D)

The dilute alleles, like those at the albino locus, affect the intensity of coat and eye colour. However, they do it by an entirely different mechanism, namely through clumping of pigment granules wherever they are secreted, rather than by an actual decrease in number of granules as in the albino allele. The concentration of pigments into irregular groups leads to a greatly decreased light absorption so that black coat looks grey. This clumping of pigment is associated with an abnormal nucleopetal melanocyte morphology. Rats with the dilute mutation produce normal types and quantities of pigment in their melanocytes but the transport of those pigments to the hair shaft is disrupted. Many melanosomes with their pigments are stuck in the cell centre, unable to be transported out to the cell edge. Hence, less pigment is incorporated in the hair, and even when it is incorporated it tends to be deposited in clumps. This gives the coat a washed-out, diluted colour (Wu *et al*., 1998).

2.4.5. White spotting

The patterns of white spotting are added independently to any coloured background in mammalian

species. In mice the piebald (S) locus has been documented to act on the differentiation of melanocyte at the neural crest, as well as on their migration to rest of the body (Jackson, 1994). The result is an array of white regions on otherwise pigmented mice. The specific colour of the pigmented regions is governed by the other coat colour loci, so that white spotting can be superimposed over any colour pattern (Sponenberg, 1997).

2.5. Molecular genetics of melanogenesis

Molecular genetics of coat colour in farm animals relies strongly on mouse coat colour genetics. There are more than 129 genes correlated with coat colour phenotypes in mice, and less than 50% of them are still unidentified (Oetting and Bennett, 2008). After identification of genes affecting coat colour in mice, different mutations in these genes in farm animals have been reported. One of the examples is a gene identified as the extension (e) locus, called MC1R (melanocortin receptor 1). This receptor is expressed at high levels in melanocytes and plays a key role in the melanin synthesis-signalling pathway through regulating intracellular levels of cyclic AMP (cAMP). This receptor could be called a pigmentary switch—activation leads to synthesis of eumelanin (brown/black) at the expense of phaeomelanin (yellow/red). Mutations in this gene were first shown in mice (Robbins *et al*., 1993) and subsequently in cattle (Klungland *et al*., 1995), horses (Marklund *et al*., 1996), sheep (Vage *et al*., 1999) and dogs (Newton *et al*., 2000). In addition to MC1R several other genes, such as agouti-signalling-protein (ASIP) gene, tyrosinase related protein 1 (TYRP 1) and tyrosinase related protein 2 (TYRP 2) are the other genes known to influence pigmentation or pigment synthesis level. In addition, there are genes affecting melanocyte precursor migration from neural crest, melanocyte survival and development. Examples are the transcription factors (PAX 3 and MITF), tyrosine kinase receptor (KIT), a G-protein coupled receptor called endothelin receptor B (EDNRB) and its ligand endothelin 3 (EDN 3). All this provides us with a directional view of complex pigment cell and pigmentation development, wherein EDNRB signalling precedes KIT signalling, which in turn precedes MC1R signalling in a serial pathway (Jackson, 1997).

3. Classification of horse coat colours

Specific combinations of point colour and body colour determine horse colour names. In horse colour terminology, the points are the mane, tail, lower leg and ear rims. The importance of the concept of the points is that their colour usually determines the name given to the overall colour combination on the horse. The two main groups of horse colours are those with black points and those with non-black points. Non-black points are usually red or cream but occasionally are brown (Sponenberg, 1996).

Colours in horses exist in considerable variety and many combinations, often demanding a close study for correct identification. As a rule, however, the colours are readily recognizable. They may be grouped and described as given below

i. Basic colours: They are black, bay and chestnut
ii. Diluted colours: They are cream, dun, silver dapple, champagne
iii. White-based colours: They are classified further based on presence of mixture of white hairs (colours includes grey, roan and white) or white patches. White patches colours include tobiano, overo and leopard (or) appaloosa complex.

Lauvergne *et al*. (1991) proposed a new descriptive scheme of horse colours with four dimensions. This system does not imply any *a priori* knowledge of the genetic formula, as it has been planned for use when nothing or little is known of the genetic background of animals in a given population. They are i) pigmentary pattern (which deals with the symmetric partition of eumelanic and phaeomelanic pigmented areas); ii) eumelanic type (black or brown); iii) pigment alteration (a modification of pigmentary appearances inside the hair by dilution or an intermixing of white and pigmented fibres); and iv) white designs (when the white patches are clearly distinct from the coloured ones).

Study on coat colour inheritance of horses was first reported by Pearson (1901) and then by Harper (1905). Later, Hurst (1906) reported the mode of inheritance for coat colours of horses viz., grey, black, bay and chestnut from the stud book records of Thoroughbred horses. Most of the remaining factors (left out by Hurst) responsible for different coat colours of horses were studied and reported by prominent early geneticists (Wilson, 1910; Sturtevant, 1910; Anderson, 1914; Wentworth, 1914; Wright, 1917). They confirmed Hurst's proposals and continued the theme of conducting genetic research on horses using available breeding records, not by experimental breeding programmes. These works were refined, compiled and new colour patterns and their modes of inheritance were identified by later workers (Gremmel, 1939; Salisbury, 1941; Salisburry and Britton, 1941; Castle, 1948; Castle and

King, 1951; Odriozola, 1951; Castle and Smith, 1953; Adalsteinsson, 1974; Van VIeck and Davitt, 1977; Sponenberg, 1982; Woolf, 1989; Bowling, 1994). Recently genome scanning and comparative genome approach was used to study the genes responsible for different coat colours in horses. The different coat colour genes and their symbols are presented in Table 1.

3.1. Basic colours

The three basic colours of horses are black, bay and chestnut (Gremmel, 1939; Salisbury, 1941). They may be described as below

Black: Black horses have black body and black points without any light areas.
Bay: Bay refers to horses with black points and shades varying from tan to brown body colour.
Chestnut: Chestnut horses have some shades of reddish body colour and have non-black points.

The genetic control of black, bay and chestnut colours of horses resides at two genetic loci, namely Extension (E) and Agouti (A) loci (Table 2). The extension locus has two alleles (E and e), that are responsible for the production of black or brown pigmented (eumelanin) and yellow or red pigmented (phaeomelanin) horses. The allele E extends the amount of eumelanin and diminishes the amount of phaeomelanin in coat and the allele e has an opposite effect. In the extension locus E allele is dominant over allele e. Hence, the genotypes EE and Ee produce black or bay and ee produces chestnut.

Table 1
Coat colour genes and symbols for different horse colours

Colour	Locus	Alleles
Chestnut	Extension (E)	Eumelanin (E)
		Phaeomelanin (e)
Bay/black	Agouti (A)	Bay (A)
		Black (a)
Palomino/buckskin/ cremello/perlino	Cream (C)	Cream dilution (C^{Cr})
		Full colour (C)
Dun	Dun (D)	Colour dilution (D)
		Full colour (d)
Silver dapple	Silver dapple (Z)	Colour dilution (Z)
		Full colour (z)
Champagne	Champagne (Ch)	Colour dilution (Ch)
		Full colour (Ch^{+})
Grey	Grey (G)	Grey (G)
		Non-grey (g)
White	White (W)	White (W)
		Full colour (w)
Roan	Roan (Rn)	Roan (Rn)
		Non-roan (rn)
Tobiano	Tobiano (To)	Tobiano (To)
		Non-Tobiano (to)
Overo	Overo (O)	Overo (O)
		Not overo (o)
Leopard spotting	Leopard spotting (Lp)	Leopard spotting (Lp)
		No leopard spotting (lp)

Table 2
Interaction of the common alleles at the extension and agouti loci

Extension genotype	Agouti genotype	Coat colour
E_	A_	Bay
E_	aa	Black
ee	A_	Chestnut
	aa	

Agouti locus is named after a South American rodent, agouti, which shows terminal or sub-terminal band of yellow colour in hairs and the rest of them have black or brown pigment (Searle, 1968). Agouti locus controls the relative distribution of black or brown areas on the horses. Between the two alleles, the dominant (A) allele restricts black to the points resulting in bay horses and the recessive allele (a) results in uniformly black horses.

The agouti genotypes AA and Aa produce bay horses and aa produces black horses. However, presence of a dominant allele at the extension locus (E) is needed for the expression of agouti alleles. The genotype ee results in chestnut colour regardless of alleles at the agouti locus. The homozygous recessive extension locus (ee) completely masks the expression of agouti locus and the mode of inheritance is called as recessive epistasis. However, Castle (1951), Dreux (1966b) and Sponenberg and Weise (1997) reported dominant black in horses and this might be due to mutation in an extension locus (E to E^{D}). Even though agouti and extension loci control eumelanin production, they do not appear to be genetically linked (Sturtevant, 1912; Wright, 1917; Gremmel, 1939; Salisbury, 1941; Castle, 1948; Bowling, 1996). Among the basic colours, bay is the most frequent horse colour and is present in all the breeds except Friesian, Fjord, Percheron, Haflinger and Suffolk Punch. The bay colour has been eliminated by selection in these breeds. The Cleveland Bay breed consists of bay horses only. Chestnut is also common in most breeds of horses, although it is rare in Highland, Percheron and Andalusian breeds. Suffolk Punch is all chestnut in colour. Black colours are rare in most breeds, although the colour does occur in most breeds except Haflinger, Fjord, Cleveland Bay and Suffolk Punch. However, some breeds like Friesian and Merens are usually black and others like Percheron and Lipizzan are grey but are generally black at birth (Sponenberg, 1996).

3.1.1. Modification of basic colours

Three of the most common modifications of the basic colours are shade, sooty and mealy.

3.1.2. Shade

This is a phenomenon that describes variations within a basic colour group resulting from light to dark shades of body colour. It is under complex, multifactorial genetic control (Sponenberg, 1996). These modifications are most noticeable on red and brown background colours such as bay or chestnut. On bay horses, the shade of colour can vary from a very dark red (blood bay) to a washed-out yellow (light bay). Chestnut horses likewise can vary in shade. The darkest red shades are called liver chestnut and the lighter red shades are called sandy chestnut. The effect of shade on black horses is not obvious, however, many black horses fade during summer months due to heat and sunlight and are called as summer black.

3.1.2.1. Sooty. Sooty is a kind of modification of basic colours due to presence or absence of black hairs among body hairs. Sooty effect is more conspicuous in bay horses and its effect is barely distinguishable in black horses. The genetic control of sootiness is not well documented and is also subject to modifications by environmental influences.

3.1.2.2. Mealy. Mealy modification produces pale red or yellowish areas on the lower belly, flanks, behind the elbows, inside the legs, muzzle and over the eyes. Mealy effect is a single gene effect, which is dominant and symbolized as Pa^{+}. The recessive non-mealy allele is Pa^{np}. Mealy effect is important in chestnut group of horses. Chestnut horses with mealy effects are called sorrel. Sorrel colour horses will have lightest shade of chestnut (yellow with a tint of red) and all other shades are called chestnut (Salisbury, 1941). However, McCann (1916) reported that sorrel is recessive to chestnut and mating among sorrel horses gives sorrel offspring only. Sorrel colour is rare in most breeds but common in American Belgian Draft horses in which chestnut is rare. Mealy effect on black horses produce seal brown colour i.e., black with light areas in muzzle, flank, under eyes and inside of the upper legs (Gremmel, 1939; Salisbury, 1941). Modification of basic colour by shade, sooty and mealy is presented in Table 3.

3.1.3. Point colour in chestnut and sorrel horses

Chestnut and sorrel horses will have non-black points. Mane and tail of this colour can vary widely. The darkest mane and tails are nearly black and the lightest mane and tail are called flaxen (i.e., nearly white). This is an independently inherited trait and occurs on each of the shades of chestnut (Salisbury, 1941). However, Castle (1948) reported that a special gene i.e., F (Flaxen) was responsible for light mane in chestnut and sorrel horses. On the contrary, Sponenberg (1996) reported that it is a polygenic trait.

Table 3
Modification of basic colour by shade, sooty and mealy

Modifier	Bay	Chestnut	Black
Shade	Most affected—produces range of colours from light to dark shades		Less affected
Sooty	Most conspicuous		Not distinguishable
Mealy	Affected	Produces sorrel colour	Produces seal brown colour

3.1.4. Colours built from the basic colours

Dilution of basic colours of horses as a result of colour dilution genes resulted in extensive array of possible colours of horses. Coat colour dilution in horses is due to the actions of four genes located at different loci. They are cream dilution, dun, silver dapple and champagne.

3.1.4.1. Cream dilution. The most widespread and familiar of the horse colour dilution gene is the one that produces the golden body colour. The horses with golden body colour are called palomino or buckskin based on the colour of the points. Palomino horses have a white (flaxen) mane and tail and buckskin have black mane, tail and legs (Salisburry and Britton, 1941; Adalsteinsson, 1974).

> Palomino: The colour of palomino may be described as yellow shades varying from cream to orange, but its distinctive features is the very light colour of mane and tail. The ideal body colour of palomino is golden yellow just like a new-minted gold. (Castle, 1948; Castle and King, 1951; Castle and Singleton, 1961).
> Buckskin: The buckskin name comes from the colour of tanned deer hide, which approximates the body colour of a buckskin horse (Jones, 1982). Buckskin horses have a yellow body and black points.

The colour of the points indicates that the palomino is a genetically modified (diluted) chestnut or sorrel (have non-black points) and the buckskin is a modified bay (have black points). The allele of the cream locus (C), is responsible for the colour dilution. The cremello allele, C^{Cr}, at the cream locus in heterozygous condition ($C\ C^{Cr}$) dilutes red to yellow resulting in bay becoming buckskin and chestnut becoming palomino. The cremello allele (C^{Cr})

shows incomplete dominance, diluting phaeomelanin and brown eumelanin to yellow but having little or no effect on black eumelanin (Salisburry and Britton, 1941; Castle, 1948; Odriozola, 1951; Castle and Singleton, 1961). The C^{Cr} allele does not affect black pigment in heterozygous condition. Whereas in homozygous condition (C^{Cr} C^{Cr}) both eumelanin and phaeomelanin pigments are diluted to cream colour (Singleton and Bond, 1966; Adalsteinsson, 1974) and the diluted horses are called as cremello or perlino depending on the colour of the points.

Cremello: Cream-coloured coat (ivory) with pink skin and blue eyes. It is a diluted chestnut horse.
Perlino: Ivory body hairs, pink skin and blue eyes. Mane and tail are darker than body. It is a diluted bay or black horse.

The phenotypes and genotypes of the diluted colours are as follows

Phenotype	Genotype
No dilution	CC
Palomino/Buckskin	C C^{Cr}
Cremello/Perlino	C^{Cr} C^{Cr}

Palomino/buckskin occurs in a variety of breeds. It is typically associated with ponies and stock horses. This dilution gene is absent in Arabians. The cremello and perlino are sensitive to sun and need protective covering. The benefit derived from cremello and perlino breeding stock is that they can produce palominos and buckskins 100% of the time. Cremello crossed with sorrel/chestnut will always produce a palomino and perlino crossed with bay or sorrel will always produce either a buckskin or palomino.

3.1.4.2. Dun. Dun gene dilutes both eumelanin and phaeomelanin. The red body colour is diluted to pale red or yellow-red and black body colour is diluted to mouse-grey.

- In bay animal, dun allele produces a more or less yellow-red animal with black points with primitive markings and is known as buckskin dun or dun.
- In chestnut horses, dun produces a pinkish red horse with darker red points with primitive markings and is called as red dun or claybank dun.
- In black horses, dun gene produces mouse-grey colour with black points along with primitive markings and is called as grulla.

The dominant allele at dun locus (D) dilutes the body colour and leaves the points unaffected and the head is darker than the body. The genotypes DD and Dd produce dun colour and dd produce non-dun horses. In addition to pigment dilution, the gene produces primitive marks (Van VIeck and Davitt, 1977). Primitive marks are probably an integral part of the action of gene at dun locus, because they are minimally present in horses that lack "D" allele. Dorsal stripe, shoulder stripes and leg bars are the common primitive markings and are controlled by a separate locus (M), which is having a close linkage with D locus (Stachurska, 1999). The dorsal stripe and markings on front legs are inherited in dominant manner. The D allelic effects can be confused with those of cremello allele (CCr), however, there are several important differences.

They are:

a. D allele dilutes both eumelanin and phaeomelanin in the body but does not dilute either pigment on the points.
b. In addition to dilution, a characteristic of D allele is the presence of primitive marking.
c. Homozygosity for D allele does not produce extreme colour dilution.

The dun is commonly present in Norwegian Fjord, Spanish breeds from North and South Americas and rare in the Arabian and Thoroughbred. The dun trait is generally found in breeds that also have cremello allele (Bowling, 1996).

3.1.4.3. Silver dapple. A third colour diluting gene, silver dapple was first described by Castle and Smith (1953). It is due to a dominant gene (Z) at silver dapple locus. This gene affects only black pigment and leaves red pigment unchanged. As a result of presence of dominant gene, black coat colour is diluted to chocolate or black-chocolate and the mane and tail are diluted to silver grey or flaxen. The diluted bay horses are called as silver-maned chestnut or silver bay. This gene has little effect on chestnut coat colour beyond producing a silver mane and tail and is called as silver sorrel, but it is difficult to distinguish from sorrel. Castle and Smith (1953) reported that the silver dapple gene (Z) in association with grey gene (G) accelerates the whitening effect of G, so that Z–G-genotype colt may be born white or become so at an age of 1 or 2 years and is called as grey-white. This colour dilution is most conspicuously found in Shetland, Miniature and Icelandic breeds and very rare in Arabian horses.

3.1.4.4. Champagne. This is a rare coat colour dilution observed in Tennessee Walking horses (Sponenberg

and Bowling, 1996). The champagne dilution results in animals with pale coat colours, mottled grey skin and amber eyes. Body colour varies from light brown to gold or cream. Eye colour of champagne is blue and darkens to amber with age. They generally lack primitive marks. In black horses, champagne dilution results in a pale brown horse with dark brown mane, tail and legs (Classical champagne colour). On a bay background it produces yellow colour with brown points (Amber champagne) and on a chestnut background it produces gold or yellow colour with yellow points (Gold champagne). The genetic control of champagne group of colours is due to a dominant gene (Ch) at champagne locus. This allele dilutes black to brown and red to yellow. The recessive wild type allele (Ch^{+}) allows expression of fully intense colours. In combination with cremello allele (C^{Cr}), the gene shows additive interaction and resulting colour appears to be indistinguishable from a cremello and is called as ivory champagne. The effect of coat colour dilution gene on basic colours is presented in Table 4.

3.2. White-based colours

3.2.1. Mixture of white hairs

3.2.1.1. Grey. Grey horses are generally born any colour, depending on the genes present at the other loci controlling coat colour. Soon after birth, a foal with grey gene will begin to show intermixed white hairs, particularly in the head (hair coat around eye sockets) and progressively acquire white hairs throughout the coat as they age. The spread of the greying process varies from horse to horse and also varies between breeds. Arabians and Welsh Ponies usually grey very rapidly and Percheron tends to grey more slowly. This is the result of independent modifiers. The grey coat colour is due to the presence of dominant gene (G) at the grey locus. The genotype of grey horses will be either GG or Gg and the horse without grey gene is symbolized as gg. Grey is epistatic to all coat colour genes except white and grey horse must have at least one grey parent (Sturtevant, 1912; Wright, 1917; Castle, 1948). Grey is the predominant colour in Arabian horses. The percentage of Arabian horses with grey, chestnut and bay are 57.8, 33.2 and 3.4% respectively (Al-Diwan and Al-Jassim, 1988). The defects associated with grey horses are melanoma. It is more prevalent in grey than non-grey horses. Grey melanomas are dermal accumulations of melanocytes and melanophages and similar to benign mole of human being. The tumors are most commonly seen on the ventral surface of the tail and peri-anal region and also on the head, neck, parotid gland and external genitalia. About 95% of melanomas are benign, but may be disfiguring. Approximately, 80% of grey horses have melanomas (Sutton and Coleman, 1997; Swinburne *et al*., 2002).

Table 4
Effect of dilution genes on basic colours in horses

Basic colour	Cream dilution	Dun	Silver dapple	Champagne
Bay	Buckskin (Heterozygote)	Buckskin dun or dun	Silver maned chestnut or silver bay	Amber Champagne
	Perlino (Dominant homozygote)			
Black	Perlino (Dominant homozygote)	Grulla	Black-chocolate	Champagne
Chestnut	Palomino (Heterozygote)	Red dun or claybank dun	Silver sorrel	Gold or yellow champagne
	Cremello (Dominant homozygote)			

3.2.1.2. Roan. Roan coloured horses have an admixture of white hairs on any colour background. In its classic expression, the roan horses has a 50% mixture of white and coloured hairs on the body (Gremmel, 1939), but the head, mane, tail and lower legs are solid coloured without mixture. Roan is a type of congenital, non-progressive silvering i.e., roan effect does not progressively whiten with age as does grey. Hair growth in areas of skin wounds may not show white hair mixture. The names given for specific combination of roan with basic colours are:

Basic colour	Roan variants
Black	Blue roan
Bay	Strawberry roan
Chestnut/ sorrel	Red roan

Roan is due to a dominant gene (Rn) at roan locus and this combines with any basic colour to produce the various shades of roan pattern. The dominant homozygote (RnRn) is lethal *in utero*. Hence all roan horses are heterozygotes and mating among them results in roan and non-roan foals in the ratio of 2:1 (Castle, 1948; Hintz and Van Vleck, 1979). Grey and roan could easily be confused; however the head and legs are darker in colour than the body in roans but not in greys. Grey horses are lighter in each shedding. Roan allele is present in Quarter Horse, Welsh Pony, Miniature and Belgian Draft, but not found in Thoroughbred and Arabians.

Roan is part of linkage group II (LG II) along with white spotting gene, tobiano (To); black-pigmented extension (E) and certain proteins such as esterase, vitamin-D binding protein and albumin (Andersson and Sandberg, 1982; Sponenberg *et al*., 1984).

3.2.1.3. White. Sturtevant (1912) apparently first recognized the occurrence of dominant white in horses and assigned the symbol "W". Salisbury (1941) reported that white coat was due to a single dominant gene and it was epistatic to all other colours and later Castle (1948) suggested that homozygosity for W was lethal. Pulos and Hutt (1969) confirmed the above finding and concluded that the autosomal gene "W" in homozygous condition (WW) was lethal and hence all horses showing dominant white were heterozygous. The heterozygous white horses lack pigment in skin and hair and hence they have pink skin, white coat, mane, tail and white hooves and eyes are usually dark brown. The mating of two white horses produces white and coloured foals in the ratio of 2:1 instead of 3:1. This might be due to death of embryo or foetus with WW genotype early in gestation. White colour occurs in few breeds viz., Tennessee Walking Horse, American Albino and Miniature but rarely in Thoroughbred and Arabian breeds. The differences between the white and cremello/perlino horses are presented in Table 5.

3.2.1.4. White patches. There are two types of white body patches. They are

a. Irregular, asymmetric patches consisting of white spotting on the body. This consists of two groups. They are tobiano and overo
b. Pattern of symmetrical spotting
   Leopard complex (or) Appaloosa complex

3.2.1.4.1. Tobiano. The general pattern of tobiano is that all four legs are white, at least below the hocks and knees, and the white spotting on the body usually crosses the topline some where between the ears and tail. As a rule the head of tobiano horses are minimally marked (as that of solid coloured horse) and have dark eyes. Tobiano is a dominantly inherited pattern of white spotting on any background colour. The tobiano pattern is due to the action of a dominant allele (To) at tobiano locus. The genotype for a horse with tobiano pattern is either ToTo or Toto (Klemola, 1933; Castle, 1954). The tobiano gene is absent in Quarter Horse, Thoroughbred, Standardbred and Arabian. But it is present in rich variety of breeds like Paint, Pinto, Tennesse Walking Horse, Icelandic, Shetland and Miniature.

Table 5
The differences between the white and cremello/perlino horses are

Character	White	Cremello/Perlino
Birth colour	White	Cream to white
Eye colour	Dark	Blue
White markings	Not visible	Visible
Genetic base colour	Any colour	Chestnut and sorrel/ bay and black

3.2.1.4.2. Overo. Overo is a Spanish word meaning "like an egg". The characteristic overo pattern features are

a. White originates on the underside of the horse and rarely cross the back of the horse between its withers and tail.
b. Generally at least one and often all the four legs will be darker in colour.
c. Head markings are predominantly white.
d. Eyes are usually brown but blue or partially blue are also present (Bowling, 1994).

The different overo patterns are

a. Frame overo: The feet and legs are usually dark, although white feet and white leg marks are common. The heads are extensively marked with white colour and eyes are blue. White areas on the body are clearly delineated.
b. Sabino: This involves extensive white on legs and face and body spots are usually on the belly and rarely as white patches. It is much more common than the other patterns.
c. Splashed white: This pattern usually has white legs and the body is white ventrally. The head is extensively and most often completely white and eyes are blue. Overo can occur with any colour and with other pattern. Overo spotting is due to an autosomal allele (O) at overo locus. The genotype for a horse with overo pattern is Oo (heterozygote). The dominant homozygote (OO) is a lethal condition and the foals will die after birth. The horses without the overo pattern are homozygous (oo) for the recessive allele (Trommershausen-Smith, 1977; McCabe *et al*., 1990; Bowling, 1994). However, Sponenberg (1996) reported that frame, sabino and splashed white patterns were genetically separate and coined the gene symbols as Fr^F, Sb^S and Spl^S for frame, sabino and splashed white patterns respectively and also stated that they were inherited in an autosomal dominant fashion. The overo pattern is mostly present in Paint and Pinto horses. Overo pattern is also called as piebald (black and white) and skewbald (white with non-black colour) in Britain (Klemola, 1933).

3.2.1.4.3. Leopard complex (or) Appaloosa complex. Leopard complex of white spotting patterns in horses is symmetrical and is mainly centered over the hips. The leopard complex can be broken down into few-spot leopard, leopard, blanket with spots, varnish roan and mottled patterns. These patterns can occur in any basic colours and with other spotting genes. Single major gene acting in an incomplete dominant fashion causes the leopard complex. This gene is under the control of modifiers to create different patterns within the complex. The dominant allele is symbolized as Lp and the recessive is as lp (Sponenberg, 1982; Sponenberg *et al*., 1990). The dominant gene under homozygous condition (LpLp) produces few-spot leopards, they are largely white with only a few coloured spots. This indicated that the homozygotes for the spotting gene usually have a greater extent of white than heterozygotes. Under heterozygous condition (Lplp) it produces a different patterns of white spotting and are as follows

a. Leopard—white with circular to oval dark spots over the body.
b. Varnish roan—nearly white with darker areas over pelvic bones, hips, elbows and facial bones.
c. Blanket—symmetrical white markings over the hips and croup; and
d. Mottled—solid coloured but has white mottling of the skin around the anus, external genitalia, mouth and eyes.

Under homozygous recessive condition (lplp) it produces horse without spotting. This spotting gene is commonly present in Appaloosa and ponies of the America bred in North America.

3.2.1.5. White markings. White markings on the head and legs are prominent characteristics of horses. Usually markings have underlying pink skin. The facial marking in horses has been designated as

Star: White marking on the face above eyes
Strip: White marking from eyes to nostrils
Snip: White marking from nostrils to the lip
Chin spot: White marking on the lower lip to the chin groove (Blunn and Howell, 1936).

The white marking on the face and legs are due to genetic and non-genetic factors. Several genes are involved in producing white markings. Males are extensively marked than females. The chestnut horses have most extensive marking than black horses (Dreux, 1966a). The facial and leg markings are correlated and influenced by the same gene. Asymmetry of leg markings

Table 6
Phenotypes and their genotypes for different coat colours in horses

Phenotype	Colour gene locus											
	White	Grey	Black/red		Dilution				Pattern			
	W	G	E	A	C	D	Z	Ch	To	O	Lp	Rn
White	W-	~	~	~	~	~	~	~	~	~	~	~
Grey		G-	~	~	~	~	~	~	~	~	~	~
Bay			E-	A-	CC				toto			rnrn
Black			E-	aa								
Chestnut			Ee	~								
Tobiano (bay)			E-	A-		dd	zz	$Ch^{+}Ch^{+}$	To-	oo	lplp	
Blue roan			E-	aa					toto			Rn-
Palomino			Ee	~	CC^{cr}							rnrn
Buckskin			E-	A-	CC^{cr}							
Cremello	ww		Ee	~	$C^{cr}C^{cr}$	~	~	~	~	~	~	~
Perlino			E-	~	$C^{cr}C^{cr}$	~	~	~	~	~	~	~
Red dun		gg	ee	~		D-					lplp	
Grulla			E-	aa	CC	D-				oo		
Red few-spot leopard			ee	~		dd			toto		LpLp	
Leopard (bay)			E-	A-			zz	$Ch^{+}Ch^{+}$			Lplp	
Overo (palomino)			ee	~	CC^{cr}					O-		rnrn
Overo/tobiano (buckskin)			E-	A-	CC^{cr}				To-	O-	lplp	
Silver dapple			E-	aa	CC		Z-		toto	oo		
Champagne			E-	aa			zz	Ch-				

All horses will have a pair of alleles in each of the 12 colour loci and symbols are given in Table 1.

Table 7
Expected results of mating between horses of different colours

Parental colour	Mostly/Always	Common	Occasional	Rare
Bay × Bay	Bay	–	Chestnut Black	–
Bay × Chestnut	Bay	Chestnut	Black	–
Bay × Black	Bay	–	Chestnut Black	–
Chestnut × Chestnut	Chestnut	–	–	–
Sorrel × Sorrel	Sorrel	–	–	–
Black × Black	Black	–	Chestnut	Bay
Black × Chestnut	Bay Chestnut	–	Black	–
Cremelo × Cremello	Cremello	–	–	–
Perlino × Perlino	Perlino	–	–	–
Cremello × Sorrel	Palomino	–	–	–
Perlino × Bay	Buckskin	–	–	–
Grey × Grey	Grey	–	Other colours	–

has been observed and this has genetic basis ((Dreux, 1966a; Woolf, 1989, 1991, 1992, 1998). Markings are distinctive and extensive in Arabian, Shire and Clydesdale breeds and absent in Cleveland Bay and Friesian. The common white facial and leg markings are due to the failure of melanoblasts to migrate and proliferate in presumptive limb and facial tissues (Seidel and Elsden, 1987). The migration and proliferation of melanoblasts is due to complex genetic and non-genetic factors. Experimental evidence for the role of non-genetic factors comes from a study of monozygotic horse twins produced by embryo micromanipulation (Allen and Pashen, 1984).

Table 8
Gene homology of horse coat colour genes with other species

Horse	Other species
Extension (E)	Guinea pig, rodent, rabbit, swine, dog, cattle
Agouti (A)—Bay is the agouti colour	Widely distributed
Albino (C)	Hamster, guinea pig, mice, rabbit, dog, cat
Dun (D)—Dominant	Mouse, rabbit, rat, cat and dogs—recessive Cattle—dominant
Silver dapple (S)	Not reported in other species
White (W)	Mouse, pig, cat, sheep, poultry, swamp buffalo
Grey (G)	Mouse, dog (Poodles and Terriers)
Roan (Rn)—Dominant homozygote is lethal	Dog—dominant Cattle—Incomplete dominance Sheep (Karakul)—Dominant homozygote is lethal
Tobiano (To)	Many mammals have white spotting
Overo (O)	
Leopard spotting (Lp)	Cat, dog (Castle, 1948; Bowling, 1996)

They showed marked variation in leg markings in monozygotic twins.

The phenotypes and genotypes for different horse colours are presented in Table 6. The expected results of the different mating are presented in Table 7 and the gene homology with other species is presented in Table 8.

4. Inheritance of different coat colour genes

Study on coat colours of horses revealed some interesting modes of inheritance and provided examples of some unique and rare genetic phenomena viz., incomplete dominance (alleles in cream and leopard complex), recessive epistasis (alleles in agouti and extension loci), dominant epistasis (alleles in white, grey and other loci) and lethal condition (due to presence of dominant genes at white, roan and overo loci). The different coat colour genes and their modes of expression explained in the previous chapter have been grouped together for better understanding.

4.1. Dominant/Recessive inheritance

The coat colour genes showing dominant and recessive types of inheritance and their phenotypes are presented in Table 9.

Table 9
Dominant and recessive type of inheritance with phenotypes

Locus	Alleles	Genotypes and phenotypes
Dun	D and d (where D is dominant over d)	DD and Dd—Dun dd—Any basic colour
Silver dapple	Z and z (where Z is dominant over z)	ZZ and Zz—Silver dapple zz—Any basic colour
Champagne	Ch and Ch^+ (where Ch is dominant over Ch^+)	ChCh and $ChCh^+$—Champagne Ch^+ Ch^+—Any basic colour
Roan	Rn and rn (where Rn is dominant over rn)	RnRn* and Rnrn—Roan pattern rnrn—Non-roan pattern
Tobiano	To and to (where To is dominant over to)	ToTo and Toto—Tobiano spotting toto—Full colour without spotting
Overo	O and o (where O is dominant over o)	OO* and Oo—Overo spotting oo—Full colour without spotting

* Lethal.

4.2. Incomplete dominance

The genes with incomplete dominance and their genotypes are presented in Table 10. The allele at the cream locus (C) is responsible for normal colour and the cremello allele at the cream locus (C^{cr}) is responsible for colour dilution and both alleles show incomplete dominance. The C allele in homozygous condition (CC) produces normal colour and in combination of cremello allele (C C^{cr}) produces palomino or buckskin horses because of partial expression of cremello allele. The cremello allele in homozygous condition (C^{cr} C^{cr}) results in complete dilution of normal colour and the diluted horses are called as cremello or perlino depending on the colour of the points. Similarly the allele at the leopard complex shows incomplete dominance.

Table 10
Genes with incomplete dominant gene action and their phenotypes

Locus	Alleles	Genotypes and phenotypes
Cream locus	C and C^{Cr}	CC—Normal colour C C^{Cr}—Palomino or buckskin based on the colour of the points C^{Cr} C^{Cr}—Cremello or perlino based on the colour of the points
Leopard complex	Lp and lp	LpLp—Few-spot leopard Lplp—Leopard spotting lplp—Non-spotted horses

4.3. Epistasis

The two different types of epistatic gene action observed in horses are recessive and dominant epistasis.

4.3.1. Recessive epistasis e.g. black, bay and chestnut colour (interaction between extension and agouti loci)

The genetic control of the above colours of horses resides at two genetic loci namely extension (E) and agouti (A) loci. The agouti genotype AA and Aa are bay horses and aa produces black. However, the presence of a dominant allele at the extension locus (E) is needed for the expression of agouti allele (A). The ee genotype at extension locus results in chestnut colour regardless of alleles at the agouti locus. The homozygous recessive extension locus (ee) completely masks the expression of agouti locus and hence the mode of inheritance is called as recessive epistasis. The detailed description of genotypes and phenotypes are presented in Table 2.

4.3.2. Dominant epistasis

i) Dominant white gene (W) at the white locus is epistatic over all loci (interaction of white and all other loci)
ii) Dominant grey gene (G) at the grey locus is epistatic over all loci except white gene (interaction of grey and all other loci except white locus).

The white colour in horses is due to a single dominant gene (W). Presence of only one of the dominant gene (W) at white locus is enough for suppressing the expression of other colour genes at different loci and hence it is called dominant epistasis. The dominant white gene is epistatic to all other genes located at different loci. Similarly the grey coat colour is due to the presence of dominant gene (G) at the grey locus. The dominant grey gene (G), at the grey locus masks the expression of genes producing different colours from the other loci except the gene for white.

4.4. Polygenic inheritance

This type of inheritance is noticed in different colour patterns of horses. They are discussed in the following sections.

4.4.1. Shade

This is the condition that describes variation within a basic colour group resulting from light to dark shades of body colour. These variations might be due to involvement of multiple genes.

4.4.2. Mane and tail colour of chestnut, sorrel and palomino horses

The colour of the mane and tail of chestnut, sorrel and palomino horses vary widely from darkest (nearly black) to lightest (nearly white) and it might be due to the influence of several genes.

4.4.3. White markings on face and legs

White markings on the head and legs are prominent characteristics in horses. The area and extent of white markings vary between horses. Several genes are assumed to be involved in producing white markings in horses.

4.5. Additive gene action

This type of gene action is noticed between following genes discussed in the following sections.

4.5.1. Cremello (C^{Cr}) and champagne (Ch) genes

The champagne dilution caused by dominant allele (Ch) at champagne locus, results in animals with pale

coat colours. However, in combination with cremello allele (C^{Cr}) the gene shows additive action resulting in a colour indistinguishable from a cremello.

4.5.2. Silver dapple (Z) and grey (G) genes

Silver dapple gene (Z) in association with grey gene (G) accelerates the whitening effect of grey gene, so that horses with Z_G-genotype may be born white or become so at an age of 1 or 2 years. On the other hand, horse without dominant silver gene, the greying process takes more time.

4.5.3. Tobiano (To) and overo (O) genes

Tobiano and overo genes produce irregular white patches on the body. Presence of the dominant genes at each locus (To at tobiano locus and O at overo locus) shows additive gene action resulting in extensive white colour.

4.6. Modifiers or modifying genes

There are instances in which a group of organisms with the same genotype for a particular gene and raised under similar environmental conditions will yet show some variation in the expressivities of the character involved. This may be due to the effect of other genes (background genotype) which influence the same character and are called as modifying genes. The variation in greying process, tobiano spotting, overo spotting, leopard complex and leg and facial markings among horses of the same phenotype might be due to the action of modifying genes.

4.7. Lethal conditions

Lethal genes produce an effect which deviates so greatly from the normal, resulting in death. Lethal genes vary considerably in the time at which they exert their lethal effect. Some cause death of the zygote or embryo while others have their effect in later stages. Lethal conditions are present in following genotypes in horses:

Dominant white gene in homozygous (WW) condition is lethal and the foetus dies *in utero*.

Dominant roan gene in homozygous condition (RnRn) is lethal and the foetus dies *in utero*.

The overo lethal syndrome due to dominant homozygotes (OO) at the overo locus results in death of the foals a few days after birth.

4.8. Linkage

Trommershausen-Smith (1978) first reported that tobiano gene (To) was linked to albumin locus (Alb^B). Later, Andersson and Sandberg (1982) reported that three coat colour genes (To, e and Rn) and three serum proteins (Albumin, esterase and group specific component-Vitamin-D binding protein) were linked together and the proposed gene order was Alb, Gc, Rn, To-e-ES. Bowling (1987) reported that there was no recombination between To, Gc and Alb and the tobiano horses mostly had Alb^B and Gc^S and the association of Gc with To was more than Alb and also proposed an equine linkage group II (LG II) with five loci namely Es, E, To, Gc and Alb. The tobiano horses had tightly linked ($To:Gc^S:Alb^B$) marker complex. Sponenberg *et al*. (1984) reported a fairly close linkage between roan (Rn) and extension (E) loci and reported a recombination rate of 0.035 ± 0.024.

5. Molecular genetic studies

During recent years, comparative genomics and whole genome scanning have been used to develop DNA tests for different variety of horse colours. Gene maps and comparative approaches have been used to assign several coat colour traits and inherited disorders to horse chromosomes. Recent molecular genetic studies on coat colour in horses helped in identification of the genes and mutation responsible for coat colour variants. In addition, microsatellite markers linked to the trait were also identified. The molecular genetic variations identified for different horse coat colours are presented in Table 11.

5.1. Extension

Melanocortin-1receptor (MSHR or MC1R) controls the level of enzyme tyrosinase in melanocytes. If the melanocyte stimulating hormone (MSH) binds with the receptor (MSHR or MC1R), the level of tyrosinase is increased. Tyrosinase is the limiting enzyme in melanin synthesis i.e. high levels of tyrosinase result in production of eumelanin (black or brown) while low levels result in the production of phaeomelanin (red or yellow). A missense mutation in the MC1R gene (C to T which leads to phenylalanine instead of serine) is associated with chestnut colour. As a result of the mutation, MSH fails to bind with MC1R, which results in low tyrosinase activity and production of phaeomelanin. All chestnut horses are homozygous for this mutation, which confirms the recessive status of the phenotype (Marklund *et al*., 1996). The MC1R gene is mapped in ECA3p. The MC1R gene is the extension locus.

5.2. Agouti

Agouti locus has two alleles (A and a), and they are responsible for production of bay (AA and Aa) and

Table 11
Molecular variations for different coat colours in horses

Colour	Chromosome	Linkage	Gene	Mutation	Variation	Reference
Extension (Chestnut)	ECA 3p	–	MC1R	C to T	Ser to Phe	Marklund *et al*. (1996)
Agouti (Black)	ECA22q15-q16	–	ASIP	11 bp deletion	–	Rieder *et al*. (2001)
Cream	ECA21q	–	MATP	G to A	Asp to Asn	Locke *et al*. (2001); Mariat *et al*. (2003)
Overo	ECA17q23-q24	–	EDNRB	TC to AG	Ile to Lys	Metallinos *et al*. (1998) and Yang *et al*. (1998)
Grey	ECA25	CORO080	–	–	–	Henner *et al*. (2002); Locke *et al*. (2002)
Appaloosa	ECA1q	ASB08 1CA43	–	–	–	Terry *et al*. (2004)
Sabino	ECA3q22	–	KIT	T to A	Skipping—exon 17	Brookes and Bailey (2005)
White	ECA3q22	ASB23	KIT	SNP polymorphism in inton 3	–	Mau *et al*. (2004)
Tobiano	ECA3q22	RFLP	KIT	–	–	Brookes *et al*. (2002)
Roan	ECA3q22	–	KIT	79 bp insertion	–	Marklund *et al*. (1999)
Silver dapple	ECA6q23	–	PMEL 17	C to T	Arg to Cys	Brunberg *et al*. (2006)
Dun	ECA8	ASB14 LEX023	–	–	–	Bricker *et al*. (2003)

black (aa) coat colours in horses in the presence of dominant allele (E) at the extension locus. Using the candidate gene strategy, polymorphism was sought in horses in agouti-signalling-protein (ASIP) gene, supposed to be involved in black colour in mice. In a 4994-bp genomic fragment of ASIP gene in horses, a deletion of 11 nucleotides (in the second exon of the gene), inducing a frameshift mutation was found to be completely associated with black colour in horses. The deletion was found to be homozygous and exactly associated with recessive black colour in horses (Rieder *et al*., 2001).

5.3. Cream

Mariat *et al*. (2003) reported that the MATP (membrane associated transfer protein) gene is responsible for cream coat colour in horse. A transition mutation (G to A) localized in exon 2 of the MATP gene leading to an aspartic acid to asparagine substitution in the encoded protein. This conserved mutation was also described in mice and humans.

5.4. Grey

Melanocyte protein 17 (PMEL 17) and tyrosinase related protein 1 (TYRP 1) show that mutation in silver and brown loci of mouse resulted in progressive greying of hair. Rieder *et al*. (2000) studied these two genes and found striking difference in mRNA expression of PMEL 17 and TYRP 1 gene and reported that they were involved in progressive greying of horses. However, further studies mapped grey locus in ECA25 therefore excluding TYRP 1 and PMEL 17 as candidate genes since they were mapped in ECA6 and ECA23 respectively. Grey locus is located very close to microsatellite marker CORO080 (Locke *et al*., 2002; Swinburne *et al*., 2002; Henner *et al*., 2002). There are no obvious candidate genes for progressive greying and melanoma development and the grey phenotype is caused by a mutation in a novel gene (Pieldberg *et al*., 2005).

5.5. Roan

Linkage study revealed zero recombination between roan and tyrosinase kinase receptor (KIT) gene. In KIT gene a 79 base pairs insertion between exons 1 and 2 (frameshift mutation) has been partly associated with roan phenotype. However, definite evidence of causative mutation is lacking (Marklund *et al*., 1999). Roan gene in cattle has been found to be linked to KIT and the same gene is also responsible for white colour in mice and pigs.

5.6. White

Molecular genetic studies revealed that the white colour in horses was linked to the microsatellite marker ASB23 in chromosome 3 and with the help of this marker the white locus was mapped in horse

chromosome 3q22. In horses, the tyrosine kinase receptor gene (KIT) involved in melanogenesis, hematopoiesis and gametogenesis was also mapped in the same region (3q21-22). Sequence analysis of KIT gene revealed a single nucleotide polymorphism (SNP) in KIT intron 3 (KITSNPIn3) associated with white phenotype in horses. The association of SNP polymorphism in KIT gene with white phenotype and mapping of the KIT gene in the same region of the white locus suggest that the KIT gene as the major candidate locus for white phenotype in horses (Mau *et al*., 2004).

5.7. Tobiano

Molecular genetic analysis of the proto-oncogene c-kit (KIT) gene (associated with white colour in horses) revealed that a polymerase chain reaction-restricted fragment length polymorphism (PCR-RFLP) pattern was associated with tobiano spotting. This polymorphism was identified in intron 13 of the equine KIT gene by comparing DNA sequences from horses with solid coat colour and horses homozygous for the tobiano spotting (To) gene. The gene associated with solid coat colour was designated KM0, while its allele for tobiano pattern (polymorphism in intron 3) was designated KM1. PCR-RFLP studies demonstrated that all 129 of 129 tobiano patterned horses possessed the KM1 allele. However, three of 104 solid-coloured Thoroughbred horses also possessed the KM1 allele. Hence, the KM1 was strongly associated with the gene for To; however the association was not absolute (Brookes *et al*., 2002).

5.8. Overo

Overo lethal white syndrome is present in humans (Hirschsprung disease), rats and mice. In these species, EDNRB gene was found to be responsible for these affections. Sequencing of horse EDNRB-DNA revealed a di-nucleotide (TC to AG) mutation, which changed isoleucine to lysine in position 118 of the protein. Sequence comparison of the horse EDNRB gene with human, rat, mouse and bovine genome revealed a high degree of homology (85–91%). Single dose of a mutant allele is enough to produce the characteristic coat colour but the presence of at least one normal allele protects against the development of aganglionosis (Yang *et al*., 1998; Metallinos *et al*., 1998).

5.9. Sabino

DNA sequence analysis of the KIT gene of horses was made for identifying its relationship with sabino pattern in horses. Genomic sequencing of the KIT gene revealed an SNP caused by a base substitution for T with A in intron 16. A complete linkage was observed between this SNP and sabino pattern in horses. All horses homozygous for this SNP were white and horses with one copy of this SNP exhibited sabino pattern. This indicated that the SNP (A to T) found within intron 16 was responsible for sabino pattern in horses (Brookes and Bailey, 2005).

5.10. Dun colour

To map dun, two Quarter Horse families segregating for the trait were screened using a genome scan comprised of 85 microsatellite markers spanning the 31 horse autosomes. The results of this scan demonstrated linkage of dun to two markers on horse chromosome 8 (ECA8) i.e., ASB14 and LEX023. In addition, chromosome specific analysis on a total of six Quarter Horse families confirmed the linkage of Dun to the group of ECA 8 microsatellite markers. Candidate genes for Dun have not yet been identified by comparative mapping analysis (Bricker *et al.,* 2003).

5.11. Silver dapple

Silver dapple in horse is characterized by dilution of the black pigment in the hair. The effect of the mutation is most visible in the long hairs of the mane and tail, which are diluted to a mixture of white and grey hairs. Using information from other species, Brunberg *et al*. (2006) carried out sequencing of pre-melanosome protein 17 (PMEL 17) gene in silver and non-silver horses. The study revealed a missense mutation in exon 11 changing the amino acid from arginine to cysteine (Arg618Cys). This mutation showed complete association with the silver phenotype across multiple horse breeds, and was not found among non-silver horses. One additional mutation located in intron 9 (only 759 bases from the missense mutation) also showed complete association with the silver phenotype. They concluded that one could find several non-causative mutations completely associated with the silver mutation but the missense mutation (exon 11) was more likely to be causative for silver colour phenotype. Subsequently, Reissmann *et al*. (2007) sequenced 1559-bp genomic fragment of silver homologous (SILV) gene in 24 horses to identify its association with silver phenotype. Among the five SNPs detected in that gene, two of the SNPs (i.e., A>T at 697 bases and C>T at 1457 bases) were completely associated with the silver phenotype.

5.12. Appaloosa/Leopard complex

The appaloosa coat colour pattern in horse is similar to that caused by the rump-white (Rw) gene in the mouse. It is a result of an inversion in the proto-oncogene c-kit (KIT). It is mapped in ECA3q21. However, studies on relationship between KIT and Lp gene revealed that KIT is not the gene responsible for appaloosa spotting in horses since Lp locus is localised in horse chromosome 1 (ECA1q). Lp is located in the interval between the microsatellite markers ASB08 and 1CA43 (Terry *et al*., 2001, 2004).

6. Conclusions

Horse colours are mostly controlled by genes at 12 different loci. The basic set of colours, black, bay and chestnut are due to the actions of genes at extension and agouti loci. The collection of colours is extended with colour dilution genes such as cream, dun, silver dapple and champagne and also with white pattern genes at white, grey, roan, tobiano, overo and leopard spotting loci. Till date no sex-linked coat colour inheritance has been reported in horses unlike in mice, Syrian hamster and cat.

Recent developments in molecular tools have given access to DNA information and provide genotypes of the animals. The most significant application so far has been for parentage testing. The molecular genetic basis of disease associated with the coat colour viz., overo white foal syndrome has been identified and genetic counselling has been provided by different dedicated laboratories to reduce the incidence or possible occurrence of this dominant trait. Allele specific tests allow owners to choose sire and dam combinations that avoid production of genetically defective offspring. Some of the colours of the foal at the time of birth is confusing because of the presence of different colour patterns and only with minor variations; however with the recent molecular genetic techniques the colour patterns such as chestnut, black, cream, overo, sabino, tobiano, white, roan and silver dapple could be identified accurately. However, further studies are needed to identify the genes responsible for other colour patterns viz., grey, dun, champagne, appaloosa/leopard complex and dominant black colours, variable colour patterns due to shade, scooty and mealy effects, white markings in the face and leg and mane and tail colour variations of the chestnut, sorrel and palomino horses.

The generation of complete genome sequence of horses will contribute to unravelling the genetic basis of phenotypic variation namely mutation and biochemical pathways associated with normal and mutated genes that affect coat colour and associated traits. This will be applied in breeding programmes to reduce the incidence of disease and to increase the production efficiency. In future it is assumed that the rapidly expanding genomic data will facilitate the identification of genes involved in complex traits.

References

Adalsteinsson, S., 1974. Inheritance of the palomino color in Icelandic Horses. J. Heredity 65, 15–20.

Al-Diwan, M.A., Al-Jassim, A.F., 1988. Morphological aspects of Arab horses in Iraq. Indian J. Anim. Sci. 58, 396–398.

Allen, W.R., Pashen, R.L., 1984. Production of monozygotic (identical) horse twins by embryo micromanipulation. J. Reprod. Fertil. 71, 607–613.

Anderson, W.S., 1914. The inheritance of coat colour in horses. Ky. Agric. Exp. Stn. Bull. 180, 119–145.

Andersson, L., Sandberg, K., 1982. A linkage group composed of three coat color genes and three serum protein loci in horses. J. Heredity 73, 91–94.

Blunn, C.T., Howell, C.E., 1936. The inheritance of white facial markings in Arabian horses. J. Heredity 27, 293–299.

Bowling, A.T., 1987. Equine linkage group II: phase conservation of To with Alb and Gc^S. J. Heredity 78, 248–250.

Bowling, A.T., 1994. Dominant inheritance of overo spotting in Paint horses. J. Heredity 85, 222–224.

Bowling, A.T., 1996. Horse Genetics. CAB International, Wallingford, United Kingdom.

Bowling, A.T., 2000. Genetics of colour variation. In: Bowling, A.T., Ruvinsky, A. (Eds.), CABI Publishing, Wallingford, U.K., pp. 53–70.

Bricker, S.J., Penedo, M.C.T., Millon, L.V., Murray, J.D., 2003. Linkage of the dun coat color locus to microsatellites on horse chromosome 8. Plant and Animal Genomes XI Conference, January 11–15, 2003, San Diego, Canada.

Brookes, S.A., Bailey, E., 2005. Exon skipping in the KIT gene causes a sabino spotting pattern in horses. Mamm. Genome 16, 893–902.

Brookes, S.A., Terry, R.B., Bailey, E., 2002. A PCR-RFLP for KIT associated with tobiano spotting pattern in horses. Anim. Genet. 33, 301–303.

Brunberg, E., Andersson, L., Cothran, G., Sandberg, K., Mikko, S., Lindgren, G., 2006. A missense mutation in *PMEL17* is associated with the Silver coat color in the horse. BMC Genet. 7, 46.

Castle, W.E., 1948. The ABC of color inheritance in horses. Genetics 33, 22–35.

Castle, W.E., 1951. Dominant and recessive black in mammals. J. Heredity 42, 48–49.

Castle, W.E., 1954. Coat colour inheritance in horses and in other mammals. Genetics 39, 35–44.

Castle, W.E., King, F.L., 1951. New evidence on the genetics of the palomino horse. J. Heredity 42, 60–64.

Castle, W.E., Smith, F.H., 1953. Silver dapple, a unique color variety among Shetland ponies. J. Heredity 44, 139–145.

Castle, W.E., Singleton, W.R., 1961. The palomino horse. Genet. 46, 1143–1150.

Cattanach, B.M., 1999. The Dalmatian dilemma: white coat colour and deafness. J. Small Anim. Pract. 40, 193–200.

Dreux, P., 1966a. Introduction statistique a la genetique des merques blanches limitees chez le cheval domestique. Ann. Genet. 9, 66–72.

Dreux, P., 1966b. Contribution a letude du gene E chez le cheval domestique. Ann. Genet. 9, 168–170.
Dring, L.A., Hintz, H.F., Van Vleck, L.D., 1981. Coat colour and gestation length in Thoroughbred mares. J. Heredity 72, 65–66.
Gremmel, F., 1939. Coat color in horses. J. Heredity 30, 437–445.
Harper, C.H., 1905. Studies in the inheritance to the theory of evolution. Volume 8. On the inheritance of coat colour in horses. Biol. Bull. 9, 265.
Henner, J., Poncet, P.A., Guerin, G., Hagger, C., Stranzinger, G., Rieder, S., 2002. Genetic mapping of the (G)-locus, responsible for the coat colour phenotype progressive graying with age in horses (*Equus caballus*). Mamm. Genome 13, 535–537.
Hintz, H.F., Van Vleck, L.D., 1979. Lethal dominant roan in horses. J. Heredity 70, 145–146.
Horstadius, S., 1950. The Neural Crest: Its Properties and Derivatives in the Light of Experimental Research. Oxford University Press, London. Cited by Searle, 1968.
Hurst, C.C., 1906. On the inheritance of coat colour in horses. Proc. Royal Soc., Ser. B 77, 388–394.
Jackson, I.J., 1994. Molecular and development genetics of mouse coat colour. Annu. Rev. Genet. 28, 189–217.
Jackson, I.J., 1997. Homologous pigmentation mutations in human, mouse and other model organisms. Hum. Mol. Genet. 6, 1613–1624.
Jones, W.E., 1982. Genetics and Horse Breeding. Lea and Febiger, Philadelphia, p. xiii+660.
Klemola, V., 1933. The "pied" and "splashed white" patterns in horses and ponies. J. Heredity 24, 65–69.
Klungland, H., Vage, D.I., Gomez-Raya, L., Adalsteinsson, S., Lien, S., 1995. The role of melanocyte-stimulating hormone (MSH) receptor in bovine coat color determination. Mamm. Genome 6, 636–639.
Lauvergne, J.J., Silvestrelli, M., Langlois, B., Renier, C., Poirel, D., Galizzi Vecchiotti Antaldi, G., 1991. A new scheme for describing horse coat colour. Livest. Prod. Sci. 27, 21–229.
Locke, M.M., Ruth, L.S., Million, L.V., Penedo, M.C.T., Murray, J.D., Bowling, A.T., 2001. The cream dilution gene, responsible for the palomino and buckskin coat colours, maps to horse chromosome 21. Anim. Genet. 32, 340–343.
Locke, M.M., Penedo, M.C.T., Bricker, S.J., Million, L.V., Murray, J.D., 2002. Linkage of the grey coat colour locus to microsatellite on horse chromosome 25. Anim. Genet. 33, 329–337.
Mariat, D., Taourit, S., Guerin, G., 2003. A mutation in the MATP gene causes the cream coat colour in the horse. Genet. Sel. Evol. 35, 119–133.
Markert, C.L., Silvers, W.K., 1956. The effect of genotype and cell environment on melanoblast differentiation in the house mouse. Genetics 41, 429–450.
Marklund, L., Johansson, M.M., Sandberg, K., Andersson, L., 1996. A missense mutation in the gene for melanocyte-stimulating hormone receptor (MC1R) is associated with the chestnut coat color in horses. Mamm. Genome 7, 895–899.
Marklund, S., Moller, M., Sandberg, K., Andersson, L., 1999. Close association between sequence polymorphism in the KIT gene and the roan coat color in horses. Mamm. Genome 10, 283–288.
Mau, C., Poncet, P.A., Bucher, B., Stranzinger, G., Rieder, S., 2004. Genetic mapping of dominant white (W), a heterozygous lethal condition in the horse. J. Anim. Breed. Genet. 121, 374–383.
McCabe, L., Griffin, L.D., Kinzer, A., Chandler, M., Beckwith, J.B., McCabe, R.B., 1990. Overo lethal white foal syndrome: equine model of aganglionic megacolon (Hirschsprung disease). Am. J. Med. Genet. 36, 336–340.
McCann, L.P., 1916. Sorrel color in horses. J. Heredity 7, 370–372.
Metallinos, A.T., Bowling, D.L., Rine, J., 1998. A missense mutation in the endothelin-B receptor gene is associated with lethal white foal syndrome: an equine version of Hirschsprung disease. Mamm. Genome 9, 426–431.
Moellmann, G., Slominski, A., Kuklinska, E., Learner, A.B., 1988. Regulation of melanogenesis in melanocyte. Pigment Cell Res. 1, 79–87.
Moyer, F.H., 1960. Some effects of pigment mutations on the fine structure of mouse melanin granules. Anat. Rec. 138, 372.
Newton, A.L., Wilkie, J.M., He, L., Jordan, S.A., Metallinos, D.L., Holmes, N.G., Jackson, I.J., Barsh, G.S., 2000. Melanocortin 1 receptor variation in the domestic dog. Mamm. Genome 11, 24–30.
Oetting, W.S., Bennett, D.C., 2008. Mouse coat color genes. International Federation of Pigment Cell Societies. . http://ifpcs.med.umn.edu/micemut.htm; (accessed 20-Apr-2008).
Odriozola, M., 1951. On the Colours of the Horse, a Guide to their Varieties and a Syndicate of Inquiry into the Mode of their Origin [A los Colores del Caballo]. Publicaciones del Sindicato Nacional de Ganaderia, Madrid, p. 435.
Pearson, K., 1901. Mathematical contributions to the theory of evolution. On the inheritance of coat colour in horses. Philos. Trans. R. Soc. 8 (195), 79.
Pieldberg, G., Mikko, S., Sandberg, K., Andersson, L., 2005. Comparative linkage mapping of the grey coat colour gene in horses. Anim. Genet. 36, 390–395.
Pulos, W.L., Hutt, F.B., 1969. Lethal dominant white in horses. J. Heredity 60, 59–63.
Reissmann, M., Bierwolf, J., Brockmann, G.A., 2007. Two SNPs in the SILV gene are associated with silver coat colour in ponies. Anim. Genet. 38, 1–6.
Rieder, S., Stricker, C., Joerg, H., Dummer, R., Stranzinger, G., 2000. A comparative genetic approach for the investigation of ageing grey horse melanoma. J. Anim. Breed. Genet. 117, 73–82.
Rieder, S., Taourit, S., Mariat, D., Langlois, B., Guerin, G., 2001. Mutation in the agouti (AS1P), the extension (MC1R) and the brown (TYRP 1) loci and their association to coat colour phenotypes in horses (*Equus caballus*). Mamm. Genome 12, 450–455.
Robbins, L.S., Nadeau, J.H., Johnson, K.R., Kelly, M.A., Roselli-Rehfuss, L., Baack, E., Mountjoy, K.G., Cone, R.D., 1993. Pigmentation phenotypes of variant extension locus alleles result from point mutations that alter MSH receptor function. Cell 72, 827–834.
Robins, A.H., 1991. Biological Perspective on Human Population. Cambridge University Press, Cambridge, United Kingdom.
Russell, E.S., 1948. A quantitative histological study of the pigment found in the coat colour mutants of the house mouse. II. Estimates of total volume of pigment. Genetics 33, 228–236.
Salisbury, G.W., 1941. The inheritance of equine coat colour—II. The basic colors and patterns. J. Heredity 31, 235–240.
Salisburry, G.W., Britton, J.W., 1941. The inheritance of equine coat color—I. The dilutes, with special reference to the palomino. J. Heredity 31, 255–260.
Searle, A.G., 1968. Comparative Genetics of Coat Colour in Mammals. Logos Press, London. 308 pp.
Seidel Jr., G.E., Elsden, R.P., 1987. Why identical twins may be different. Hoards Dairyman 132, 740.
Singleton, W.R., Bond, Q.C., 1966. A allele necessary for dilute coat colour in horses. J. Heredity 57, 74–77.
Sponenberg, D.P., 1982. The inheritance of leopard spotting in the Noriker horse. J. Heredity 73, 357–359.
Sponenberg, D.P., 1996. Equine Coat Color Genetics. Iowa State University Press, Ames.

Sponenberg, D.P., 1997. Genetics of colour and hair texture. In: Piper, L., Ruvinsky, A. (Eds.), The Genetics of Sheep. CABI Publishing, Wallingford, pp. 51–86.

Sponenberg, D.P., Bowling, A.T., 1996. Champagne, a dominant colour dilution of horses. Genet. Sel. Evol. 28, 457–462.

Sponenberg, D.P., Weise, M.C., 1997. Dominant black in horses. Genet. Sel. Evol. 29, 403–408.

Sponenberg, D.P., Harper, H.T., Harper, A.L., 1984. Direct evidence for linkage of roan and extension loci in Belgian horses. J. Heredity 75, 413–414.

Sponenberg, D.P., Carr, G., Simak, E., Schwink, K., 1990. The inheritance of the Leopard complex of spotting patterns in horses. J. Heredity 81, 323–331.

Stachurska, A.M., 1999. Inheritance of primitive markings in horses. J. Anim. Breed. Genet. 116, 29–38.

Stachurska, A., Pieta, M., Lojek, J., Szulowska, J., 2006. Performance in racehorses of various colours. Livest. Prod. Sci. 106, 282–286.

Staricco, R.G., 1963. Amelonotic melanocytes in the outer sheath of the human hair follicle and their role in repigmentation of regenerated epidermis. Ann. N.Y. Acad. Sci. 100, 239–255.

Sturtevant, A.H., 1910. On the inheritance of coat color in American Harness horses. Biol. Bull. 19, 204–216.

Sturtevant, A.H., 1912. A critical examination of recent studies on colour inheritance in horses. J. Genet. 2, 41–51.

Sutton, R.H., Coleman, G.T., 1997. Melanoma and the greying horse. RIRDC Res. Pap. Ser. 55, 1–27.

Swinburne, J.E., Hopkins, A., Binns, M.M., 2002. Assignment of the horse grey coat colour gene of ECA25 using whole genome scanning. Anim. Genet. 33, 338–342.

Terry, R.R., Bailey, E., Bernoco, D., Cothran, E.G., 2001. Linked markers exclude KIT as the gene responsible for appaloosa coat colour spotting patterns in horses. Anim. Genet. 32, 98–101.

Terry, R.B., Archer, S., Brookes, S., Bernoco, D., Bailey, E., 2004. Assignment of the appaloosa coat colour gene (LP) to equine chromosome 1. Anim. Genet. 35, 134–137.

Trommershausen-Smith, A., 1977. Lethal white foals in mating of overo spotted horses. Theriogenology 8, 303–312.

Trommershausen-Smith, A., 1978. Linkage of tobiano coat spotting and albumin markers in a pony family. J. Heredity 69, 214–216.

Vage, D.I., Klungland, H., Lu, D., Cone, R.D., 1999. Molecular and pharmacological characterization of dominant black coat color in sheep. Mamm. Genome 10, 39–43.

Van VIeck, L.D., Davitt, M., 1977. Confirmation of a gene for dominant dilution of horse colors. J. Heredity 68, 280–282.

Wentworth, E.N., 1914. Colour inheritance in horse. Zeit. F. Abst. U. Ver. 11, 10–17.

Wilson, J., 1910. The inheritance of coat colour in horses. Proc. R. Dubl. Soc. 12, 341–348.

Woolf, C.M., 1989. Multifactorial inheritance of white facial markings in the Arabian horse. J. Heredity 80, 173–178.

Woolf, C.M., 1991. Common white facial markings in bay and chestnut Arabian horses and their hybrids. J. Heredity 82, 167–169.

Woolf, C.M., 1992. Common white facial markings in Arabian horses that are homozygous and heterozygous for allele at A and E loci. J. Heredity 83, 73–77.

Woolf, C.M., 1998. Directional and anterior asymmetry of common white markings in the legs of the Arabian horse. Genetica 101, 199–208.

Woolf, C.M., Swafford, J.R., 1988. Evidence for eumelanin and pheomelanin producing genotypes in the Arabian horse. J. Heredity 79, 100–106.

Wright, S., 1917. Color inheritance in mammals. VII: The horse. J. Heredity 8, 561–564.

Wu, X., Bowers, B., Rao, K., Wei, Q., Hammer III, J.A., 1998. Visualization of melanosome dynamics within wild-type and dilute melanocytes suggests a paradigm for myosin V function In vivo. J. Cell Biol. 143, 1899–1918.

Yang, G.C., Croaker, D., Zhang, A.L., Manglick, P., Cartmill, T., Cass, D., 1998. A dinucleotide mutation in the endothelin-B receptor gene is associated with lethal white foal syndrome (LWFS); a horse variant of Hirschsprung disease (HSCR). Hum. Mol. Genet. 7, 1047–1052.