

## Special Article

# Coat colour dilution lethal ('lavender foal syndrome'): a tetany syndrome of Arabian foals

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### Introduction

Coat colour dilution lethal (CCDL), referred to as 'lavender foal syndrome' by Arabian horse breeders, is a tetany syndrome of newborn Arabian foals of Egyptian breeding. The condition has been recognised for over 50 years but has not been described in the peer-reviewed literature. The purpose of this report is to make practitioners aware of its existence.

Aside from the neurological signs, the most striking feature of this condition is the dilute or bleached-out hair coat colour. In a few cases, the colour is a very striking iridescent silver to pale lavender hue, hence the name 'lavender foal syndrome'. Coat colour dilution lethal is a more appropriate name, as many affected foals do not exhibit the striking lavender colour. Other dilute coat colours observed are pewter (pale slate grey) and pale chestnut (pink).

### Case histories

#### Case 1

A male Egyptian Arabian foal was delivered unassisted after a normal gestation. The foal exhibited intermittent opisthotonus and paddling movements and was unable to assume sternal recumbency or stand. The suck reflex was strong. Haematology and serum biochemistry were normal. After two days of intensive supportive care with no improvement, the foal was subjected to euthanasia. Gross *post mortem* examination was normal with the exception of abrasions of prominent areas of the skull due to injury. Histology revealed splenic necrosis and depletion of lymphocytes, and lipidosis of the liver. No lesions were observed in the central nervous system (CNS). The foal was a pale chestnut with a lavender hue (**Fig 1**).

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#### Case 2

A male Egyptian Arabian foal was born unassisted. Tetanic episodes with opisthotonus and paddling movements occurred every 15 mins following birth. Between episodes, the foal would whinny for the mare. A strong suck reflex was present. The foal was unable to assume sternal recumbency or stand; it failed to improve over the next 24 h and was subjected to euthanasia. *Post mortem* examination and histopathology failed to reveal any lesions other than chemosis and abrasions over pressure points. The foal was a pale chestnut-lavender colour (**Figs 2 and 3**).

#### Case 3

A male Egyptian Arabian foal was delivered unassisted. Opisthotonus and intermittent paddling movements were observed. The foal was unable to assume sternal recumbency and was subjected to euthanasia, but was not available for *post mortem* examination. The foal's coat colour was a very pale chestnut, almost pink.

#### Case 4

A female Egyptian Arabian foal was born with assisted delivery; it was unable to assume sternal recumbency or stand



**Fig 1:** Affected foal (Case 1) exhibiting opisthotonus.



**Fig 2: Affected foal (Case 2) with normal head size and shape.**

and exhibited periodic episodes of paddling and opisthotonus. Moderate joint rigidity of the forelimbs was evident. The filly was a very pale chestnut with a slight silver hue. Euthanasia was performed and *post mortem* examination, including histopathology, revealed no lesions in the CNS or other organs except for large clumps of melanin in the hair roots and shafts.

### Case 5

A female Egyptian Arabian foal was born unassisted after a normal gestation. It was unable to stand or assume sternal recumbency, and displayed intermittent opisthotonus and paddling. The foal was subjected to euthanasia but was not available for *post mortem* examination. This foal was a very pale chestnut colour.

### Case 6

A grey female Egyptian Arabian foal with a slight lavender hue was born with an assisted delivery after a normal gestation. The foal had a strong suck reflex but was unable to assume sternal recumbency or stand. Opisthotonus, extensor rigidity and intermittent paddling were exhibited, and chemosis, corneal ulceration and abrasions over pressure points were evident. Radiographic examination of the head and neck revealed a normal skull and cervical vertebrae. After 6 days of treatment with no improvement, the foal was subjected to euthanasia. Gross and histopathological examination failed to reveal any lesions in the nervous system or other organs, with the exception of local pulmonary atelectasis and melanin clumps in the hair shafts and follicles.

## Discussion

The clinical signs of CCDL appear to represent a form of tetany from an episodic diffuse release of extensor motor neurons resulting in extensor rigidity and opisthotonus. The paddling movements may represent attempts by the foal to overcome



**Fig 3: Affected foal (Case 2) exhibiting paddling movements.**

this and gain sternal recumbency. Alternatively, these episodes may represent partial seizures due to uncontrolled neuronal activity from a prosencephalic disorder. The author favours the former interpretation, based on the character of the signs, normal sensorium and no normal periods between episodes. This entity needs to be differentiated from the signs of neonatal septicaemia (NS) and neonatal encephalopathy (NE).

Septicaemic foals are not usually affected at birth. Seizures may be seen with meningitis (Mahaffy and Rossdale 1957; Rossdale 1972). Many septicaemic foals are afebrile, but haematology will usually indicate infected foals. Blood cultures, if positive, will help elucidate septicaemic foals. CCDL foals that are kept alive for several days often show lesions of neonatal septicaemia.

Foals affected with NE often appear normal at birth but within the first 24 h show a complete and sudden loss of the suck reflex, cerebral dysfunction, seizures and/or respiratory distress. Many foals affected with NE recover, often taking up to 30 days. Those that die will usually show lesions in the CNS, lungs and possibly other organs (Rossdale 1972).

A seizure disorder seen in Arabian foals of Egyptian breeding under 12 months of age has been referred to as idiopathic (Mittel 1987) or benign (Mayhew 1989) epilepsy. Affected foals are normal at birth and between seizures. If seizures are not observed, unexplained facial trauma is evident. In some affected foals seizures appear to be induced by stress, while in others they occur spontaneously (Mittel 1987). Affected foals usually outgrow seizures by 12–18 months of age. Since foals affected with benign (idiopathic) epilepsy do not die, histopathology is unavailable. Coat colour is unaffected.

Congenital defects, including occipitoatlantoaxial malformation (OAAM), of Arabian foals should be considered (Mayhew *et al.* 1978). Foals affected with OAAM may be normal at birth and develop neurological signs shortly afterwards. While tetanic episodes are not a feature of OAAM, this condition should be considered in any Arabian foal exhibiting neurological signs at birth. Palpation and radiography of affected foals will demonstrate the malformation. Coat colour is unaffected.

Seizures may be one of the signs present with hydrocephalus. Abnormal skull shape may not be observed (de Lahunta 1977).

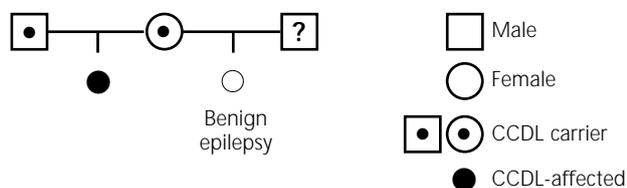


Fig 4: Pedigree of the foal in Case 1.

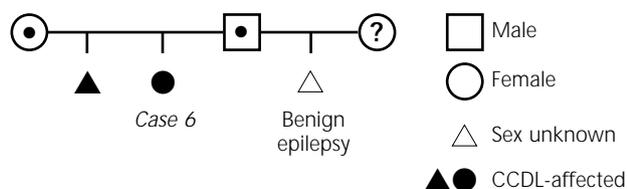


Fig 5: Pedigree of the foal in Case 6.

If the dilute coat colour and Arabian breeding are overlooked, CCDL foals are often misdiagnosed as NS or NE. CCDL foals kept alive with supportive treatments do not show any improvement and are subjected to euthanasia.

Alteration of hair colour has been associated with several diseases in animals and man, including Chediak-Higashi syndrome in cattle, mink, cats, mice and man (Leader *et al.* 1965; Witkop *et al.* 1978), canine cyclic haematopoiesis or gray collie syndrome (Guilford 1987), cerebellar Purkinje cell degeneration and coat colour dilution in Rhodesian Ridgeback dogs (Chieffo *et al.* 1994), overo lethal white syndrome (OLWS) of Paint horses (Vrotos *et al.* 2001) and copper deficiency, both primary and secondary, of cattle and sheep (Saunders 1983).

With the exception of OLWS and copper deficiency, there appears to be no known connection between the dilute coat colour and the underlying pathophysiology of the other syndromes. OLWS of Paint horses is due to a substitution of lysine for isoleucine at residue 118 of the endothelin receptor B or endothelin 3. The endothelin pathway is necessary for the migration of melanocytes and enteric neurons from the neural crest (Vrotos *et al.* 2001). Unlike OLWS, with CCDL there is no lack of migration of melanocytes, but rather a defect within the pigment cells. In copper deficiency, the alteration in hair colour is due to failure of the conversion of tyrosine to melanin, which is catalysed by the copper-containing enzyme tyrosinase. The copper-deficient foal, however, does not show hair colour dilution, possibly due to a lower copper requirement (Bridges *et al.* 1984).

The possible relationship of CCDL to benign epilepsy of Arabian foals cannot be dismissed. Both conditions occur in Arabian foals of Egyptian breeding. The author is aware of 2 Egyptian Arabian horses that have produced both CCDL and benign epilepsy foals; the mare that produced the filly described in Case 1 also produced a bay filly with benign epilepsy when bred to a different stallion. The coat colour of the bay filly was normal (Fig 4). The bay filly affected with benign epilepsy exhibited periodic seizures, quivering, walking

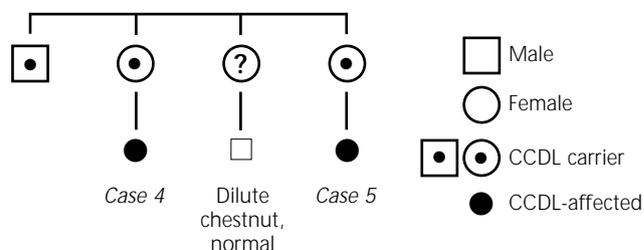


Fig 6: Pedigree of the foals in Cases 4 and 5.

in circles and jaws clamped shut, but was normal between seizures. The seizures ceased by 12 months of age. The stallion that sired the filly in Case 6 also produced a foal with benign epilepsy when bred to a different mare (Fig 5). These instances raise the question as to whether CCDL is a more severe form of benign epilepsy involving a more complex mode of inheritance, or whether they are two distinct entities. Another confusing factor is the normal male foal, half-sibling to the foals in Cases 4 and 5, with a dilute chestnut coat that gradually darkened with age. It is not known whether CCDL was somehow involved for this normal foal, or an unrelated coincidence (Fig 6). While most of the evidence would suggest a simple autosomal recessive mode of inheritance (Bowling 1996), the factors described here suggest a more complicated inheritance.

In view of the fact that CCDL may be an inherited anomaly, regardless of the mode of inheritance, to prevent the spread of this condition carrier mares and stallions should not be used for breeding.

Foals affected with CCDL present with many signs that are exhibited by polled Hereford calves with inherited congenital myoclonus due to an inherited glycine receptor deficiency in motor neuron cell bodies of the spinal cord that innervate the extensor muscles (Harper *et al.* 1986; Gundlach *et al.* 1988; Pierce *et al.* 2001). A similar inherited myoclonus due to glycine receptor deficiency in spinal cord neurons has been reported in purebred Peruvian Paso horses (Gundlach *et al.* 1993). Some of these horses, unlike CCDL foals and polled Hereford calves, were able to stand and walk. No lesions, gross or microscopic, have been found in any of the above. Affected polled Hereford calves and Peruvian Paso horses were hypersensitive to sensory stimuli.

There is indirect evidence that tetany of polled Hereford calves occurs *in utero*. Tetany has not been observed in CCDL foals *in utero*; it appears to be initiated *post partum*, possibly an attempt by the foal to right itself. Breeders of Arabians who have produced CCDL foals have stated that no abnormal discomfort of the mare or violent *in utero* activity by the foal were observed during the last trimester of pregnancy. Due to the length of the foal's limbs, the close confinement of the foal within the uterus and the sometimes rather violent nature of the tetanic episodes, one would expect an occasional mare to have a ruptured uterus. The author has not heard of any mare with this injury with a CCDL foal.

Based upon the sparse evidence presently available and the lack of gross or microscopic lesions, this syndrome (CCDL)

appears to be a biochemical lesion of the central nervous system involving the release of lower motor neurons. Glycine receptors and neurotransmitters and their metabolites in CCDL foals are areas that should be explored thoroughly.

CCDL should be included in the differential diagnosis of any newborn Arabian foal of Egyptian breeding with a markedly dilute coat colour exhibiting a seizure-like disorder at birth.

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