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Plants Associated with Congenital Defects and Reproductive Failure (3-Mar-2004)

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Considerable livestock losses occur annually as the result of toxic plants that cause embryonic death, abortion, and fetal abnormalities [1-3]. Plant toxins also interfere with reproduction through their effects on male fertility, especially by affecting spermatogenesis. The plant species that have been historically associated with abortion and infertility in livestock are listed in Table 8-1. Those plant toxins capable of causing fetal death or deformity are referred to as teratogens. To be a teratogen, a plant toxin must readily cross the placenta at a high enough dose and be present at a specific time in gestation to exert its effect on the developing fetus [3,4]. In addition, susceptibility to a plant teratogen depends on the animal species, because not all species are equally susceptible to teratogens. In general, the fetus is most susceptible to teratogens during the first trimester of pregnancy. The western false hellebore (*Veratrum californicum*) is a classical example of a teratogen because it only induces the cyclops deformity in lambs if the pregnant ewe eats sufficient quantity of the plant during the 13 - 14th days of gestation [5]. Other than plant teratogens, viruses, nutritional imbalances and deficiencies, chemicals (nitrates), and radiation may also be teratogenic and must be considered when determining the cause of congenital deformities. The plants that have been confirmed or suspected of being teratogens in animals are listed in Table 8-2.

Teratogenic Plants

Milk Vetches and Locoweeds -

In general, the milk vetches or locoweeds (*Astragalus* and *Oxytropis* spp.) have the greatest economic impact on animal reproduction compared to any other group of plants. Most of the 370 or more species of milk vetch and locoweeds thrive in the more arid and alkaline areas of western North America. Relatively few of these species, however, are known to be toxic and those that are more commonly associated with livestock poisoning are discussed under locoism in Chapter 6. Swainsonine, one of a group of indolizidine alkaloids found in the poisonous milk vetches and locoweeds, is the principle toxin responsible for causing reproductive problems in animals that eat them [6]. The alkaloid affects almost all organs because it inhibits normal cellular energy metabolism. Consequently swainsonine has a profound effect on all aspects of the reproductive system in both females and males.

Table 8 - 1. Plants Associated with Livestock Abortion	
Scientific Name	Common Name
<i>Amaranthus</i> spp.	Red-rooted pigweed
<i>Agave lecheguilla</i>	Lechuguilla
<i>Astragalus</i> spp.	Milk vetch, locoweeds
<i>Brassica</i> spp.	Rape
<i>Conium</i> spp.	Poison/spotted hemlock
<i>Cupressus</i> spp.	Cyprus
<i>Festuca</i> spp.	Fescue
<i>Gutierrezia sarothrae</i>	Broomweed, snakeweed
<i>Halogeton</i> spp.	Halogeton
<i>Indigofera glomeratus</i>	Juniper
<i>Juniperus</i> spp.	Juniper
<i>Medicago sativa</i>	Alfalfa
<i>Oxtropis</i> spp.	Locoweeds
<i>Phytolacca americana</i>	Poke weed
<i>Pinus ponderosa</i>	Ponderosa pine
<i>Solidago</i> spp.	Goldenrods
<i>Tanacetum</i> spp.	Tansy
<i>Trifolium</i> spp.	Clovers
<i>Veratrum</i> spp.	False hellebore, skunk cabbage

Cattle and sheep, and to a lesser extent horses, are the most susceptible to the reproductive and teratogenic effects of chronic locoweed poisoning [7-10]. Unlike most teratogens, swainsonine may exert its effects on the dam and the fetus at any time during gestation, causing a variety of problems. These reproductive problems are most likely due to the combined effects of swainsonine on the pituitary gland affecting gonadotrophin production, the ovary affecting estrogen and progesterone levels, the uterus and placenta, and directly on the fetus [11]. Abortion, infertility, fetal deformity, and disturbances in placental circulation that results in massive accumulation of fluid in the uterus (hydrops). Some calves and lambs may be born weak and do not thrive. Abortions can occur at anytime during gestation [9]. Animals that have aborted tend to cycle normally and will conceive again provided they are kept from eating more locoweed, and there is not a chronic secondary uterine infection resulting from the abortion.

Common fetal deformities encountered in livestock eating locoweeds include twisted and deformed limbs resulting from contracted flexor tendons of the legs, and abnormal development of the bones and joints. These congenital defects are identical to those produced by lupines, poison hemlock and members of the family Solanaceae such as wild and cultivated tobacco. Lambs born to ewes eating locoweed during the 60th to 90th day of pregnancy may develop enlarged hearts and thyroid glands. Using ultrasound technology, it is possible to detect the effects of swainsonine on the formation of cotyledons of the placenta, heart enlargement and irregularity in the heart beat in fetal lamb [12]. Initially the fetal heart rate is

accelerated but then it slows and eventually stops, causing fetal death and abortion.

Locoweeds also affect reproduction by decreasing sperm production in rams and bulls [13]. Swainsonine affects the sperm producing cells of the testicles causing the formation of abnormal sperm with reduced motility, thereby severely affecting the reproductive capacity of the ram or bull eating locoweeds [13,14]. Testicular function is also affected by the action of swainsonine on the pituitary gland that alters normal gonadotrophin levels [15]. These changes are not permanent, and normal spermatogenesis returns after a period of 60 - 90 days once the animal has stopped eating milk vetch or locoweed [13].

In those areas of North America where milk vetch and locoweeds are prevalent, poisoning from these plants should always be considered as a cause for reproductive failure and congenital abnormalities in livestock. It is however difficult to confirm a diagnosis of locoweed poisoning as the cause for a reproductive problem as the effects of the plants are likely to be encountered long after the plants were consumed.

Table 8 - 2. Known and Suspected Teratogenic Plants	
Scientific Name	Common Name
<i>Astragalus</i> spp.	Milk vetch, locoweed
<i>Blighia sapida</i>	Akee
<i>Colchicum autumnale</i>	Autumn crocus
<i>Conium maculatum</i>	European or spotted hemlock
<i>Cycadaceae</i> spp.	Cyads
<i>Datura stramonium</i>	Jimson weed
<i>Indigofera spicata</i>	Creeping indigo
<i>Lathyrus</i> spp.	Wild pea
<i>Leucaena leucocephala</i>	Mimosa
<i>Lupinus</i> spp.	Lupine
<i>Nicotiana glauca</i>	Wild tree tobacco
<i>Nicotiana tabacum</i>	Tobacco
<i>Oxytropis</i> spp.	Locoweed
<i>Papaveraceae</i>	Poppies
<i>Senecio</i> spp.	Groundsel
<i>Veratrum californicum</i>	Western false hellebore
<i>Vinca rosea</i>	Periwinkle

Freshly aborted fetuses and the placenta when examined histologically may show the characteristic cellular vacuolation of swainsonine poisoning. The alkaloid itself can be detected in the serum of animals if they have been eating locoweed within 2 days of sampling because the serum half-life of swainsonine is only about 20 hours. Further discussion of the effects swainsonine, and the descriptions of the milk vetches and locoweeds themselves can be found in Chapter 6.

Lupine, Blue Bonnet

Lupinus spp. - Fabaceae (Legume family)

Habitat

Approximately 100 species of lupine occur in North America, ranging from the dry hills and plains to moist mountain valleys up to 11,000 feet (3,352 meters) altitude.



Habitat of Lupine, Blue Bonnet. *Lupinus* - Fabaceae (Legume family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

Lupines are perennial herbaceous plants growing up to 3 feet (1 meter) in height, with alternate, palmately compound leaves, each with 5 to 17 leaflets. The leaflets are oblanceolate smooth or hairy, especially on the underside. The showy inflorescence is a terminal raceme of compact white, blue- purple, red or yellow pea-shaped flowers (Fig.8-1A and Fig. 8-1B). The fruit is a multiseeded leguminous pod.



Figure 8-1A. Lupine (*Lupinus* spp.). - To view this image in full size go to the IVIS website at www.ivis.org . -



Figure 8-1B. Lupine showing typical palmate leaf and flowers (*L. leucophylus*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin

Most species of lupine are not toxic and are used extensively in some parts of the world as a high-protein food source for human and animal consumption. Those species that have been associated with poisoning contain quinolizidine and piperidine alkaloids in all parts of the plant. (Table 8-3). The principal teratogenic quinolizidine alkaloid in lupines is anagryne [16,17]. Drying the plants in hay does not reduce their toxicity. The mechanism by which anagryne and other alkaloids causes fetal deformity is poorly understood. Restricted fetal movement due to either general or localized uterine contraction as has been demonstrated with the coniine, the teratogenic alkaloid in poison hemlock (*Conium maculatum*), is most likely the reason the fetal calf develops the skeletal deformities seen in crooked calf disease [16,18-20].

Table 8 - 3. Lupine Species Known to Contain Anagryne [3]

Scientific Name	Common Name
<i>Lupinus. argenteus</i>	Silvery lupine
<i>L. caudatus</i>	Kellog's spurred lupine

Scientific Name	Common Name
<i>L. erectus</i>	Tall silvery lupine
<i>L. evermannii</i>	Evermans lupine
<i>L. laxiflorus</i>	Douglas spurred lupine
<i>L. leucophyllus</i>	Wooly leafed lupine
<i>L. nootkatensis</i>	Nootka lupine
<i>L. serecius</i>	Silky lupine

Crooked Calf Disease

Crooked calf disease is a well recognized syndrome in the western United States characterized by skeletal deformities in calves born to cows that consume 0.5 to 1.0 kg/day of toxic lupine species between days 40 and 70 of gestation [16,20,21,24]. Affected calves may show varying degrees of limb deformity (arthrogryposis), vertebral column malformation (scoliosis, kyphosis, torticollis), and cleft palate [20,21]. The front limbs are usually most severely affected with deformities occurring in the elbow, knee (carpus), and fetlock joints (Fig. 8-2). Unlike commonly encountered contracted tendons that are similar in appearance, crooked calf disease involves permanent bone and joint structure changes referred to as arthrogryposis. Congenital limb deformities and cleft palate are also caused by inherited genetic disorders such as occur in the Charolais breed and by viruses such as the Akabane virus that is yet to become a problem in North America [25].



Figure 8-2. Crooked legged calf (arthrogryposis) due to lupine teratogenicity. - To view this image in full size go to the IVIS website at www.ivis.org . -

Other plants capable of causing skeletal deformities in animals include poison hemlock (*Conium maculatum*) (see Chapter 1), tobacco stalks (*Nicotiana tabacum*), wild tree tobacco (*N. glauca*), and locoweeds (*Astragalus* and *Oxytropis* spp.). Mountain thermopsis (*Thermopsis montana*), a common wild flower of the Rocky Mountains, also contains anagryne and is potentially teratogenic [26]. It has been suggested that there is a risk to pregnant women who drink the milk of cows consuming lupines and other teratogenic plants because the toxic alkaloids are secreted in milk [27].

Nervous Syndrome

Lupines have been associated with three different syndromes of poisoning in livestock. In North America, lupine poisoning is most commonly associated with a teratogenic syndrome that most frequently affects cattle, and is commonly referred to as "crooked calf disease" [20,21]. Occasionally lupines have caused an acute fatal neurologic disease in sheep, and rarely in cattle and horses. The toxins responsible for the neurotoxicity are a variety of alkaloids other than anagryne. Sheep ingesting from 0.25 to 0.5 percent of their body weight of seeds from certain lupines found in the western United States develop an acute neurologic disease characterized by muscle tremors, noisy labored breathing, convulsions, coma, and death. Species of lupine that have been incriminated in this neurologic syndrome include *L. leucophyllus*, *L. argenteus*, *L. leucopsis*, and *L. siriccus* [23]. A third syndrome, lupinosis, is associated with livestock grazing lupine pods and stalks infected with a fungus *Phomopsis leptostromiformis* (*Diaporthe toxica*) that produces a mycotoxin (phomopsin) capable of causing severe liver, kidney and muscle disease [28-31]. The fungus persists in the lupine stubble after harvesting and causes severe liver disease and poor growth in sheep and occasionally cattle that graze the stubble [29-31]. Lupinosis is especially important in those parts of the world where lupines are grown for the purpose of harvesting their seeds for animal consumption [28].

Poison Hemlock, Spotted Hemlock

Conium maculatum

Poison hemlock is a widespread weed throughout most of North America, and has toxicologic significance because of its

profound effects on the nervous system and its teratogenic properties. The alkaloid coniine, found in all parts of the plant, is a potent neurotoxin and a teratogen (see Chapter 1). Cattle and pigs seem to be the most susceptible to the teratogenic effects of coniine, while horses and sheep appear to be unaffected [18-20,32]. Sublethal doses of coniine ingested by cows between the 50th and 70th days of gestation cause congenital malformations in the calf (crooked calf disease) that are indistinguishable from the teratogenic effects of tobacco (*Nicotiana* spp.) [33] and lupine (*Lupinus* spp.) poisoning [18]. Calves with crooked legs due to deformity of the bones of the carpal and hock joints (arthrogryposis) may cause difficulty in calving, as they are unable to pass through the birth canal of the cow normally. In addition the vertebrae may show varying degrees of malformation and malalignment, and a cleft palate may be present [34].

As with other congenital deformities, it is often difficult to determine the teratogen involved, because the deformity is not evident until the fetus is born many months after the plant teratogen was eaten by the dam. A presumptive diagnosis is usually possible by establishing the presence of poison hemlock in the pasture that the dam happened to be in during early pregnancy.

Plants Causing Abortion

Western False Hellebore, Skunk Cabbage, Corn Lily

Veratrum tenuipetalum (*V. californiuom*), *V. viride* - (Green false hellebore) Liliaceae (Lily family)

Habitat

Western false hellebore is more common in moist mountain meadows and valleys above 8500 feet (2,590 meters), where it can form dense stands. Green false hellebore (*V. viride*) is more common at lower altitudes in moist meadows and forested areas.



Habitat of Western False Hellebore. *Veratrum tenuipetalum* (*V. californiuom*) - Liliaceae (Lily family). -
To view this image in full size go to the IVIS website at www.ivis.org . -

Description

Both species are very similar, course, erect, 4 to 8 feet (2 to 3 meters) tall, with short perennial rootstalks. The leaves are smooth, alternate, parallel veined, broadly oval to lanceolate, up to 12 inches (3 cm) long, 6 inches (15 cm) wide, in three ranks and sheathed at the base (Fig. 8-3A). The inflorescence is a panicle of very numerous, small, greenish white, star-shaped flowers, the lower ones often staminate and the upper ones perfect (Fig. 8-3B). The flowers of *V. viride* are distinctly green. The fruit is three-chambered with several seeds.



Figure 8-3A. False hellebore (*Veratrum viride*). - To view this image in full size go to the IVIS website at www.ivis.org . -



Figure 8-3B. Western false hellebore or skunk cabbage (*V. tenuipetalum*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin

Over 50 complex alkaloids have been identified from *Veratrum* spp., some of which have been used as hypotensive drugs [35]. The plant is most toxic when it first emerges in the early spring, becoming less toxic and more unpalatable as it matures. The roots are more toxic than the leaves.

Several of the alkaloids including cyclopamine, jervine, and cyclopassine are teratogenic [36]. *Veratrum* is the classical teratogen, causing pregnant ewes that consume the plant on the 14th day of gestation to produce a lamb that has a single eye located in the center of its head (cyclopia) [5]. If *Veratrum* is eaten later in gestation (30 - 35th. day) other defects including shortened legs and tracheal agenesis may develop [37]. Embryonic death in lambs without development of cyclopia may also occur [37,38]. *Veratrum* poisoning occurs mostly in sheep, but cattle, goats, and llamas are also susceptible to the teratogenic effects of cyclopamine [5].

Clinical Signs

Veratrum tenuipetalum is primarily important because of its teratogenic effects in sheep, but if consumed in quantity over a short period of time can produce acute poisoning. Sheep eating 6 to 12 oz of the plant may within a few hours show signs of excessive salivation, vomiting, fast irregular heart rate, muscular tremors, incoordination, and coma in severe cases. There is no specific treatment, but the affected sheep should be kept quiet and given symptomatic treatment as needed until they recover.

Pregnant ewes consuming *Veratrum* spp. on the 14th day of gestation may develop characteristic cyclopia in up to 25 percent of the lambs born [5,35,39]. Affected lambs are born with varying degrees of facial deformity including cyclopia (single or double centrally located eye), protruding and twisted mandible, shortened upper jaw and proboscis-like structure located above the eye (Fig. 8-4). The lambs have been referred to as "monkey faced" because of their appearance. Ewes eating *V. tenuipetalum* between 30 and 33 days of gestation produced lambs with different deformities that included cleft palate, hairlip, shortened legs, and tracheal stenosis [37-39]. Most deformed lambs are either born dead or die shortly after birth. Prolonged gestation periods are also associated with *V. tenuipetalum* poisoning.



Figure 8-4. Cyclops lamb. - To view this image in full size go to the IVIS website at www.ivis.org . -

The teratogenic and other effects of *Veratrum* poisoning can be avoided by keeping sheep off of pastures containing the plants, especially during the first trimester of pregnancy. If this is not possible, delaying the breeding season until after the first killing frost is a way of avoiding problems because the plants die off and lose their toxicity.

Tree Tobacco

Nicotiana glauca - Solanaceae (Nightshade family)

Other Poisonous Species of Tobacco

N. trigonophylla - Desert tobacco

N. attenuata - Wild tobacco

N. tabacum - Cultivated tobacco

Habitat

Tree tobacco is a common weedy shrub of waste areas, roadsides, dry hillsides, washes and canyons at lower altitudes.



Habitat of Tree Tobacco. *Nicotiana glauca* - Solanaceae (Nightshade family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

Tree tobacco is a perennial shrub or small tree growing to 20 feet (5 to 6 meters) in height. Stems are loosely branched, with leaves that are entire, ovate, hairless, and bluish green. Flowers are pale yellow, tubular, 2 inches (4 to 5 cm) long, in loose pendant clusters at the ends of branches (see Fig. 6-26A and Fig. 6-26B). Blooms are produced throughout the year.

Principal Toxin

Many alkaloids are present in the various species of *Nicotiana*. Two distinctly different clinical syndromes can occur with *Nicotiana* poisoning depending upon the predominant active alkaloid present in the plant. Nicotine and anabasine are the 2 most active alkaloids with respect to animal poisoning. Nicotine is poisonous to all animals, although ruminants are more tolerant of the alkaloid effects than are simple-stom-ached animals. Nicotine is readily absorbed through the digestive and respiratory tracts and has a rapid effect on the nervous system, frequently causing muscle tremors, excitement, ataxia, rapid heart and respiratory rates, and coma. Death results from respiratory paralysis.

The alkaloid, anabasine, is teratogenic to pigs, lambs, and calves [40-42]. Quantitatively, anabasine forms 99 percent of the alkaloid content of *N. glauca* and will cause severe skeletal deformities in lambs and calves born to their mothers that consumed the plant during the 30th to 60th day of gestation [40,42].

Clinical Signs

Pregnant cows, ewes, and sows that consume the green plants of wild or domestic tobacco may occasionally show signs of nicotine poisoning, but it is the anabasine content of the plants that more commonly prevails to produce fetal deformities [3,40]. Anabasine, when consumed between days 30 and 60 of pregnancy, causes severe bony deformity (arthrogryposis) of the limbs and vertebrae [3,40]. Calves, lambs, and piglets are born with varying degrees of crooked legs due to malformation of the bones of the carpal, fetlock, and pastern joints [3,40-42]. Abnormal spinal curvature (scoliosis) and twisted necks (torticollis) may also occur. These same defects may also be produced by lupine (*Lupinus* spp.) [16,24] certain locoweeds (*Astragalus* and *Oxytropis* spp.), and poison hemlock (*Conium maculatum*) [18].

Broom Snakeweed, Turpentine Weed, Slinkweed

Gutierrezia sarothrae, *G. microcephala* - Threadleaf snakeweed Asteraceae (Sunflower family)

Habitat

Snakeweed is commonly found in the dry plains and hills at 4000 to 10,000 feet (1,219 to 3,048 meters) of altitude, where it can form dense stands over thousands of acres. The predominance of snakeweed in rangelands is generally indicative of over-grazing and poor range management.



Habitat of Broom Snakeweed. *Gutierrezia sarothrae*, *G. microcephala* - Threadleaf snakeweed, Asteraceae (Sunflower family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

Snakeweed is a herbaceous perennial small shrub with a woody base, growing up to 24 inches (70 cm) in height (Fig. 8-5A). The stems are branching, and the leaves are linear, alternate, and hairless. The yellow flowers are small, numerous, and in clusters at the ends of branches (Fig. 8-5B). A given flower head will have no more than three to eight small ray flowers and three to eight disc flowers. The corollas have five lobes and the pappus is composed of several to many oblong scales. Snakeweed is considered an evergreen shrub in south western North America, and is deciduous in colder areas.



Figure 8-5A. Broom snakeweed invading rangeland (*Gutierrezia sarothrae*). - To view this image in full size go to the IVIS website at www.ivis.org . -



Figure 8-5B. Broom snakeweed detail of flower and leaves (*Gutierrezia sarothrae*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Threadleaf snakeweed (*G. microcephala*) is quite similar in appearance but has smaller flowers, each with 1 to 3 disk flowers and 4 to 5 ray flowers.

Principal Toxin

Several potentially toxic compounds are present in snakeweed including steroids, terpenoids, saponins, and flavones [43]. Triterpene Saponins are thought to be the compounds responsible for the toxicity of broom snakeweed [44-47]. However, the toxicity of the plant appears to be quite variable, with animal susceptibility being dependent on the quantity of snakeweed consumed. Cattle on a good plane of nutrition can consume up to 30 percent snakeweed without apparent detrimental effect [48,49]. The green and to a lesser extent the dried plant may cause abortions in cattle, sheep, and goats at any stage of gestation [44,45].

Clinical Signs

A variety of clinical signs have been attributed to snakeweed poisoning including poor appetite, weight loss, initial diarrhea followed by constipation, jaundice, and abortions [50]. Calves near term may be born weak and die shortly after birth. Retention of the placenta is a common sequel to abortion. Swelling of the vulva and udder edema has also been associated with snakeweed poisoning. Severe cases may have uremia and blood in the urine indicative of kidney degeneration. At postmortem examination liver, kidney, and gastrointestinal lesions may be present. Diffuse toxic hepatitis with hydropic degeneration of hepatocytes and acute tubular nephrosis characterize the pathologic changes of snakeweed poisoning [51].

Western Yellow or Ponderosa Pine

Pinus ponderosa - Pinacea (Pine tree family)

Habitat

Ponderosa pines are common large trees of western North America preferring mountain slopes, valleys, and mesas, generally on south-facing slopes.



Habitat of Western Yellow or Ponderosa Pine. *Pinus ponderosa* - Pinacea (Pine tree family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

Growing to 100 feet (30 meters) in height, ponderosa pines are broad and round-topped trees with thick, orange-brown bark

that separates into scales or plates. Young trees have a dark brown or black bark. The dark green needles are 5 to 10 inches (12.5 to 25 cm) long in threes or twos and threes on the same tree and clustered near the end of branches. The cones are ovoid in shape, 3 to 6 inches (7.5 to 15 cm) long, each scale tipped with a recurved prickle (Fig. 8-6).



Figure 8-6. Ponderosa pine needles and cone (*Pinus ponderosa*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin

A variety of agents have been associated with the toxicity of pine needles including phytoestrogens, mycotoxins, resins, and lignols [51-57]. However, the principal compound in ponderosa pine needles responsible for causing premature parturition or abortion in cattle is isocupressic acid [58]. Junipers also contain significant levels of isocupressic acid. Other compounds present in the pine needles and bark of the tree including abietic and dehydroabietic acids (diterpene abietane acids) are toxic to cattle. Individually or in combination these compounds are possibly responsible for the kidney and brain degeneration described in cattle that have eaten pine needles [60]. Pregnant cattle and bison are the most likely species to abort from pine needles, while sheep, goats, and mares do not abort after eating pine needles [61].

Other species of pine tree and junipers (*Juniperus* spp.) have been suspected of causing abortion, but in North America the ponderosa pine is most frequently incriminated [62]. Pine needles from the new branch tips and the bark are the most toxic [63].

The means by which pine needles cause abortion or premature parturition is thought to be due to isocupressic acid and possibly other compounds causing a marked decrease uterine blood flow as a result of vasoconstriction [47,64,65]. This results in a change in the equilibrium of the hormones that maintain pregnancy and premature parturition results [66]. Specifically progesterone levels progressively decline as a result of necrosis of the corpus luteum [67]. The viability of the calf will depend on how close it was to term before premature delivery.

Pine Needle Abortion in Cattle

Cattle consuming pine needles in the last trimester of pregnancy will undergo premature parturition from 2 to 21 days later [62-64]. Cattle will eat pine needles when stressed or when normal forage is scarce such as during winter snowstorms. The quantity of pine needle necessary to produce premature parturition experimentally is in the range of 2.2 to 2.7 kg/day for at least 3 days [63]. Greater quantities may be readily consumed if cows in late pregnancy are without food during a winter storm. Affected cows develop edematous swelling of the vulva and udder and a mucoid vaginal discharge before premature parturition or abortion. Weak uterine contractions and uterine inertia may result in poor cervical and vaginal dilation that can result in difficulty in delivery of the calf [60,67]. Retention of the fetal membranes (placenta) and secondary uterine infections commonly occur in the cows that abort, which have serious consequences for the future fertility of the cow if it does not die from septic metritis. Some aborted fetuses may be autolyzed in utero several days before abortion. Calves that are born alive are often weak and their ability to survive is compromised by the fact that their mother often produces little or no colostrum or milk.

At postmortem examination of cows that have died from the complications of pine needle-induced premature parturition, septic necrosis of the uterus and placenta and necrosis of the corpora lutea are commonly present [67,68]. Histologically however, kidney and skeletal muscle degeneration and patchy neuronal degeneration in the brain also contribute to the syndrome of pine needle abortion [60].

Phytoestrogens

Phytoestrogens are substances found in some plants that have estrogen-like properties and compete for estrogen receptors on cells. Consequently, phytoestrogens can mimic the effects of estrogen and cause infertility. Phytoestrogens (isoflavones, coumestans) are found in legumes such as alfalfa (*Medicago sativa*), burr medic (*Medicago* spp.), red clover (*Trifolium pratense*), and subterranean clover (*Trifolium subterranean*) [69,70]. Silage made from red clover has been incriminated in an estrogenic syndrome [71]. Similar estrogenic compounds are found in soybeans [72].

Sheep in particular that graze subterranean clover pastures over a period of years develop lowered fertility that is referred to as "clover disease." A similar disease has been reported in cattle grazing burr medic that contained significant quantities of phytoestrogens [73]. This decreased flock fertility has been problematic in Australia, causing economic losses [69,74,75]. Phytoestrogens alter cellular structure and mucous consistency in the cervix, thus lowering chances of fertilization [76].

Affected sheep do not exhibit normal seasonal breeding cycles and develop cystic ovaries and irregular estrus cycles. Wethers exhibit teat enlargement when chronically exposed to phytoestrogens. Fertility returns once ewes are removed from clover pastures. Ram fertility does not appear to be affected adversely by grazing estrogenic pastures [74]. Selection of different clover species or new hybrids with low estrogen activity has reduced infertility problems associated with grazing clover pastures.

Nitrate Poisoning

Nitrate poisoning is primarily a problem of cattle and occasionally other ruminants resulting from the consumption of plants and water containing high levels of nitrates. Nitrate, is readily reduced by rumen organisms to nitrite, that once absorbed, converts hemoglobin of red blood cells to methemoglobin. As the level of methemoglobin increases, the oxygen carrying capacity of the blood decreases, with the animal eventually dying from lack of oxygen. Aside from the lethal effect of nitrate poisoning discussed in Chapter 1, pregnant cows may also abort from the effects of the nitrite. The fetus is particularly susceptible to decreases in oxygen crossing the placenta as a result of methemoglobinemia and the effects of nitrite on the maternal and fetal circulation [77,78]. Fetal death and abortion may occur at any stage of gestation as a result of the combined effects of decreased placental oxygen transport and the limited ability of the fetus to metabolize nitrite [79-81]. Abortions may also result from the decrease in progesterone production induced by chronic nitrate poisoning interfering with luteal production of progesterone [82].

Plants or hay containing 1 percent or more nitrate (10,000 ppm) dry matter are potentially toxic and should be fed with caution. Forages containing more than 1 percent nitrate should only be fed if the total nitrate intake can be reduced to less than 1 percent by diluting the nitrate-forage with nitrate-free forages. Further description of plant nitrate poisoning and the plants commonly associated with nitrate poisoning are discussed in Chapter 1.

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