UNITED STATES DEPARTMENT OF AGRICULTURE

BULLETIN No. 800

Joint Contribution from the Bureau of Animal Industry, JOHN R. MOHLER, Chief
and the Bureau of Plant Industry, WM. A. TAYLOR, Chief

Washington, D. C. PROFESSIONAL PAPER June 8, 1920

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By

C. DWIGHT MARSH and A. B. CLAWSON, Physiologists,
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CONTENTS

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PART I.—INTRODUCTION.

HISTORICAL SUMMARY AND REVIEW OF LITERATURE.

The literature relating to *Asclepias galioides* as a poisonous plant is confined to three publications. Glover and Robbins, in 1915,[1] published statements that cattle in western Colorado had been reported as being killed by a plant which they called *A. verticillata*, but that experiments with rabbits had failed to produce results. Glover, in 1917, published the results of some experiments with rabbits, from which he inferred that the plant was not poisonous either when dry or green, but added that cases reported warrant the suspicion that "the whorled milkweed may be a very dangerous poison weed for sheep and cattle." In July, 1918, Glover, Newsom, and Robbins published a somewhat detailed account of the plant and its distribution, gave the history of some cases of sheep

[1] Full titles of articles referred to in the text are given in the list of literature at the end of the paper.

poisoning in western Colorado, and described experiments in feeding sheep and rabbits which demonstrated the poisonous character of the plant.[1]

In preceding years, however, the Department of Agriculture had received many reports of losses of live stock from milkweed. In most cases the species of plant which caused the trouble was not indicated and the reports were so indefinite that the evidence was not considered strong enough to warrant the addition of the plant to the list of stock-poisoning plants. The reports came from not only Colorado but also from New Mexico, Arizona, California, and Oregon. In 1902, J. C. Johnson, of Higbee, Colo., reported the loss of horses from *Asclepias verticillata.*

In October, 1909, Dr. W. E. Howe, inspector in charge of the Denver district, received from Dr. S. C. Babson details of heavy losses of sheep in the neighborhood of Montrose, Colo. The losses were said to have been due to *Asclepias verticillata*, inasmuch as the animals had fed extensively on the plant and it was found in abundance in the stomach contents. Post-mortem examinations were made, and he reported as the only lesion "pale heart muscles, excessive amount of pericardial fluid, and acute inflammation of the outer covering of the surfaces of the brain."

A similar report was made by Dr. Babson to the chief of grazing, Forest Service, Denver, Colo. He said that the plant grew on the banks of irrigation ditches and that it had been traced from the beginning of the Montrose and Delta Canal to the California mesa. He stated, however, that the plant had leaves 3 or 4 inches long and in pairs. From the description it was assumed that the plant had been wrongly determined and that probably the species he had in mind was *Asclepias speciosa.* Some experimental work was undertaken in regard to *Asclepias speciosa* without any definite results.

The attention of the Washington office was again called to the matter by a letter from L. F. Kneipp, district forester, who reported losses of stock from *Asclepias subulata* near Diamond Valley on the Dixie National Forest and asked for an investigation. A package of the plant, which was said to have killed a great number of cattle on the Dixie Forest, was sent to the Bureau of Plant Industry for investigation, but on account of the small quantity of material it was impossible to determine whether the plant was poisonous. The accounts of the losses of animals on the Dixie Forest, however, were so definite that it was planned to make a more thorough field examination. Meantime, in 1910, Mr. Balthis, supervisor of the Alamo National Forest, sent in specimens from Alamogordo, N. Mex.,

[1] In the Amer. Jour. of Vet. Med., Vol. XIV, pp. 135–136, Dr. L. H. Pammel, in addition to a review of the bulletin by Glover, Newsom, and Robbins, reports the treatment used by a local veterinarian on sheep poisoned by whorled milkweed near Hotchkiss, Colo.

which were identified as *Asclepias galioides* or *Asclepias verticillata.* He stated that it was known in that region as the "beeweed" and that it was regarded as very poisonous to stock.

A statement was sent to the department from the Coconino National Forest, Arizona, which indicated that considerable numbers of sheep were lost in that locality from poisoning by "milkweed." Assistant Botanist Eggleston, while at Mount Carmel, southern Utah, in 1914, was told by Bishop Sorenson that he had seen calves poisoned by the whorled milkweed.

A trip was made by the senior author in 1916 to New Harmony, Utah, on the edge of the Dixie Forest, where losses were said to occur from *Asclepias subulata.*[1] Stockmen in the neighborhood of New Harmony gave somewhat detailed accounts of the deaths of both sheep and cattle from this milkweed, which grows in abundance near the irrigated lands. Arrangements were made with some of them to send a quantity of the milkweed to the experiment station at Salina, Utah, for experimental work. The material failed to arrive, and consequently the experimental work was not undertaken so early as had been planned.

In the fall of 1917 some Colorado papers gave detailed accounts of the loss of 800 sheep in the neighborhood of Dolores and it was stated that the place where the animals died had been known as a "death patch." From the Montezuma National Forest details were obtained of the losses, which, it appeared, did not occur in Dolores but just east of Cortez. It seems that losses had occurred there in preceding years, but at that time, December 7, 736 head out of 1,000 died and it was supposed that the milkweed was the cause. The locality was visited by the senior author in October, 1918, and a careful examination of the region was made in company with Gordon Parker, supervisor of the Montezuma National Forest, and County Agent Newsom. It was found that the place where the loss occurred in 1917 was an area a short distance from Cortez, in which *Asclepias galioides* grows in great abundance. Mr. Newsom said that deaths had occurred repeatedly on this area and that within 3 or 4 years from $35,000 to $45,000 worth of sheep had been lost. This case was reported also by Glover, Newsom, and Robbins. It was found that there were thick patches of the weed in other localities near Cortez, and that there had been other cases of poisoning. From stockmen it was learned also that there had been serious losses near Dolores.

The Grand Junction (Colo.) Daily Sentinel of March 20, 1918, reported that about 60 head of sheep near Whitewater, Colo., had been poisoned by hay which contained milkweed. The case was investigated in the following May by a member of the department's

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[1] It may be noted that systematic botanists have determined that the milkweed of that locality is *A. galioides*, not *A. subulata*.

force engaged in investigating poisonous plants. It was found that during lambing the sheep were fed Gunnison Valley hay which contained a considerable quantity of *Asclepias galioides*. One hundred and twenty were said to have been fed, and of that number between 50 and 60 died. The symptoms, as described by the veterinarian who was called in, comprised convulsions, rapid pulse and respiration. Nausea and considerable salivation were present. No bloating was noticed. In the autopsy the only lesion reported was hemorrhagic spots on the heart and lungs. These cases, it should be noticed, were due to the dry plant in the hay.

About the middle of June, 1918, a letter was received from Assistant District Forester Hatton referring to a heavy loss of sheep near Hotchkiss, Colo., with the suggestion that the matter might be worth more careful investigation. Hotchkiss was reached on June 14 by the senior author, and the next day, in company with Mr. Bennett, who owned the sheep, Mr. Kreutzer, the supervisor of the Gunnison National Forest, and Fred Hotchkiss, of Hotchkiss, he made an examination of the locality. It was found that 1,600 sheep had been kept on a pasture of about 40 acres in the "Midway" region for a day with no feed except that which could be grazed in the pasture. An examination of the pasture showed that the vegetation was largely sagebrush, alfilaria, and *Asclepias galioides*. A part of the pasture was an abandoned orchard in which milkweed was abundant.

The deaths of the sheep had occurred between 2 and 3 weeks before, and in consequence it was somewhat difficult to determine to what extent the milkweed had been grazed. A careful examination, however, showed that it had been eaten in many places, and as there was little else in the pasture it was assumed that the animals had eaten the weed, and that it was the cause of the loss. At that time the weed was from 8 to 15 inches high, and was in bud but with no flowers. It was stated that the animals did not die in the pasture but that symptoms began to appear 2 or 3 hours after they left it. Some of them lived 12 hours after symptoms appeared. The principal symptoms, according to Mr. Bennett, were violent convulsions, and it was said that the animals would pound their heads upon the ground. Some of the animals became sick as late as 1 o'clock the next day. The total loss was about 400, or about half of those that were sick.

The weed was found in some other localities between Hotchkiss and Paonia, and Mr. Hotchkiss remarked that he had noticed that when hungry sheep fed upon it many of the sheep died, and that when they avoided the milkweed he lost no sheep, so he felt positive that the milkweed was the cause of the loss. The evidence pointed so strongly to the milkweed that it was deemed probable that it was the real cause of the losses.

ASCLEPIAS GALIOIDES. MATURE PLANT FROM HOTCHKISS, COLO., SHOWING FLOWERS AND FRUIT.

ASCLEPIAS GALIOIDES. PLANT FROM HIGH ROLLS, N. MEX., IN FLOWER, WITH ROOT SYSTEM.

ASCLEPIAS GALIOIDES. YOUNG PLANT FROM PAONIA, COLO., IN BLOSSOM, SHOWING LONG ROOT.

A considerable quantity of the plant was collected and sent to the Salina experiment station, where experiments, which were immediately undertaken, proved it to be extremely toxic.

Assistant Botanist Eggleston spent most of July, August, and September, 1918, in investigating the distribution and habits of the whorled milkweed in Colorado, Utah, and New Mexico.

DESCRIPTION OF ASCLEPIAS GALIOIDES.

Asclepias galioides, whorled milkweed. The stems are erect, single, or several, sometimes branching, "near woody" at base, and from 1 to 5 feet high; the main roots are horizontal, often branching, with adventitious buds producing new stems; the leaves are in whorls, from 2 to 6, narrowly linear, from 2 to 4 inches long; the flowers are in umbels from one-half to 1 inch across, at the ends of branches or in the axils of leaves; the 5 greenish-white sepals are ovate, reflexed, and persistent; the petals are united; there is a crown of cornucopialike segments with horns attached between the corolla and stamens; the stamens are 5 in number, and the pollen coheres in a waxy mass which is removed bodily by insects; the pods are from 1 to 3 inches long, narrow, hairy, splitting on the sides; the seeds are flat, reddish-brown, with a tuft of long, silky hairs at summit. It flowers in June and July, the blooms often continuing until September.

Plate I illustrates the mature plant, showing both flowers and fruit. Plate II shows also the root, and Plate III shows the extended root system of even small plants. Plate IV, figure 1, shows the plant growing in an abandoned orchard.

There seems to have been some confusion in regard to the systematic position of the whorled milkweed. Glover, 1917, and Glover, Newsom, and Robbins, 1918, call it *A. verticillata*. The plant collected in southern Utah, as stated on page 3, was known as *A. subulata*. A special study of the subject was made by Mr. Eggleston with the following result:

The whorled milkweeds were named by Dr. Gray, 1886, as follows:

Asclepias mexicana.
Asclepias verticillata.
  var. *subverticillata.*
  var. *pumila.*

A. galioides was first described by Humboldt, Bonpland, and Kunth, 1818, from the State of Michoacán, Mexico.

Miss Anna M. Vail, 1898, separated the group into 7 species.

Wooton and Standley, 1915, considered *A. galioides* the common New Mexico species of whorled milkweed and then reached the following conclusions in regard to other species:

Our specimens may include *A. verticillata*, but we have been unable to separate them definitely. They also include specimens cited by various authors as

A. subverticillata. In our opinion there is only one species of this type in New Mexico.

The study of fresh specimens in New Mexico, Colorado, Utah, and the examination of dried specimens in the herbaria leads to the conclusion that *A. verticillata* does not occur in the Rocky Mountain country, but is a species of the Atlantic Plains and the Mississippi Valley.

A. mexicana grows from 3 to 5 feet high, and has wider leaves and shorter horns than other species of the whorled-milkweed group. It ranges from southern Mexico through western Arizona, California, and western Nevada to the Columbia and Snake River valleys in Washington and eastern Idaho.

A. pumila (*A. verticillata* var. *pumila*) is a low, tufted plant with leaves irregularly crowded on the stem. The plant, if it proves to be only a variety, belongs with *A. galioides.* It ranges from South Dakota to Colorado, western Nebraska, and New Mexico.

A. galioides was included by Dr. Gray in *A. verticillata.* Recent authors have tried to distinguish the two species by the shape of their hoods, describing those of *A. verticillata* as *entire* from a rear view, and those of *A. galioides* as *hastate-sagittate.*

All the whorled-milkweed flowers seen in the summer of 1918 had entire hoods. Examination of these specimens after drying shows the hoods *hastate-sagittate.* A study of herbarium specimens indicates that hoods of both *A. verticillata* and *A. galioides* are often *hastate-sagittate* when dried. These species, however, differ in two respects. *A. verticillata* has a bunch of long, fibrous roots and smooth pods; *A. galioides* has horizontal main roots and hairy pods, and in these characters agrees with *A. pumila* and *A. mexicana.* In flower the species appear to be nearly identical.

There appears to be no doubt that the plant which has been responsible for the cases of poisoning in Colorado, Utah, Arizona, and New Mexico is *A. galioides.*

DISTRIBUTION AND HABITS OF THE PLANT.

The plant ranges northward from Central America through Arizona and New Mexico to central Utah and central Colorado.

It has been found in Utah as far north as Beaver County (according to Esplin) and the foothills of the Uinta Mountains (according to Jones). In western Colorado it has been seen on Grand River as far up as Glenwood Springs, on the North Fork of the Gunnison River as far as Bowie, and on the Gunnison River to the Black Canyon.

In eastern Colorado it has not been observed north of the Arkansas watershed, but occurs on that river as far as Parkdale, just above the Royal Gorge. Figure 1 shows, in a general way, its distribution.

The natural habitat of *Asclepias galioides* is dry plains and foothills. In the foothills of Colorado and New Mexico it seems best at home in the bottoms of draws. In southern Utah it occurs frequently in sandy, rolling plains. In New Mexico it reaches an altitude of about 7,500 feet and in southern Colorado 7,000 feet.

Its downy seeds are adapted to wind dispersal, but in the irrigated orchards and fields, where whorled milkweed is becoming abundant, the rapid increase has been due largely to water transportation of seeds. The irrigating ditches have proved to be ideal for the transportation, germination, and development of seeds. Wherever ditches have been dug in the neighborhood of whorled milkweed young plants have developed along the water line and spread by means of horizontal roots and seeds. The main ditches carry seeds into the laterals and thence into the open fields. Fortunately the milkweed is a sun-loving plant and does not germinate or grow well in the shade. There is little evidence that it establishes itself in fields with heavy cover crops like alfalfa, but a poorly seeded field may be just the place for it to get a strong foothold. In old orchards where the milkweed gets a start it runs riot, often forming a solid mat between the trees.

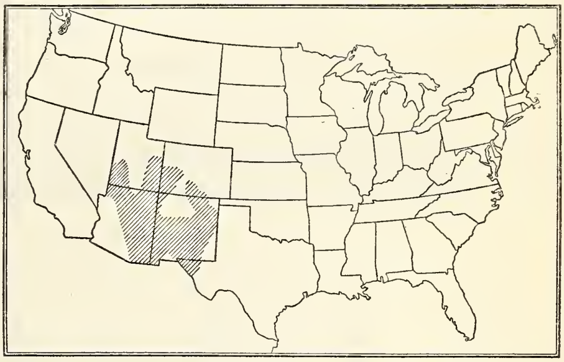

FIG. 1.—Distribution of *Asclepias galioides* in the United States.

The rapidity with which the plant spreads along the ditches is amazing. The orchard country at Grand Junction, Colo., has been ditched by various projects, the last and uppermost of which is the United States Reclamation Service ditch. Lateral ditches from this main ditch, dug in new ground but three years ago, are fringed with milkweed.

In the Grand Junction region much of the stock poisoning is caused by milkweed in the hay. The trees in many milkweed-infested orchards there have been removed and the land sown to alfalfa.

Another orchard country, on the North Fork of Gunnison River, in Delta County, Colo., has no milkweed in its hay, but heavy losses of stock are reported at the time the animals are trailed to and from the summer ranges in the mountains. Ditches and fence rows along these trails often have quantities of milkweed which the stock eat when forage becomes scarce.

Many areas in southern Utah are given up to corn raising by dry-land farming and afford another poison-milkweed problem. Some of the fields are in the natural habitat of the milkweed; cultivated soil forms a better seed bed than the undisturbed soil; cultivation breaks up the horizontal roots and propagates new plants rapidly. Areas of this type may be seen between Kanarraville and New Harmony, Utah.

On some of the overgrazed ranges whorled milkweed has become a menace to stock. The range country in Long Valley on the Virgin River near Mount Carmel, Utah, appears to be an overgrazed range of that sort. Arizona and New Mexico also have the same range trouble.

PART II.—EXPERIMENTAL WORK.

Although both cattle and horses are killed by the milkweed, the greater part of the experimental feeding work was done with sheep, since most of the heavy losses are of sheep, and, moreover, it did not seem wise to kill cattle and horses unless it was distinctly necessary. Enough was done with cattle and horses to demonstrate the toxicity of the plant for those animals and to show that the results obtained from the sheep experiments could be applied to other animals. Table 1 gives a summary of the experiments.

TABLE 1.—*Summary of feeding experiments with Asclepias galioides, 1918.*

Animal.		Date of feeding.	Method of feeding.	Part of plant used.	Weight of plant estimated as green plant for 100 pounds of animal.	Remedy used.	Result.	Where plant was obtained.	Remarks.
Designation.	Weight.								
Horse:	*Pounds.*				*Pounds.*				
No. 126	1,020	July 30	Fed in hay	Green leaves, stems, and buds.	0.22	Arecolin	Very sick, recovered.	Hotchkiss, Colo	
No. 126	990	September 20	do	Dry leaves, stems, and flowers.	.14		Not sick	Paonia, Colo	
Cattle:									
No. 815	430	August 1	do	Green leaves, stems, and buds.	.163		do	Hotchkiss, Colo	
No. 815	448	August 8	do	Dry leaves, stems, and buds.	.22		do	do	
No. 815	449	August 13	do	do	.242		do	do	
No. 815	455	August 17	do	do	.294		do	Paonia, Colo	
No. 750	575	August 22	Fed	Green leaves, stems, and flowers.	.22		do	Grand Junction, Colo	
No. 750	588	August 25	Fed in hay	Partly dry leaves, stems, and flowers.	.626		do	do	
No. 750	593	August 26	do	do	.845		Sick	do	All may not have been eaten.
No. 750	600	September 22	do	Dry leaves, stems, and flowers.	.551	Arecolin	Death	Paonia, Colo	
Sheep:									
No. 480	95.5	June 18	Balling gun	Green leaves, stems, and buds.	.577		do	Hotchkiss, Colo	
No. 478	100.5	June 19	do	do	.165		Not sick	do	
No. 476	81.5	June 20	do	do	.270		Death	do	
No. 465	121	June 21–24	Fed in hay	do	.44		Not sick	do	Not eaten.
No. 509	117	June 20	do	do	.189		do	Paonia, Colo	
....	....	June 21	do	do	.22		do	do	Ate 0.2 pound June 21.
....	....	June 22	do	do	.22		Death	do	
No. 470	93	July 2–14	Balling gun, daily feeding.	Dry leaves, stems, and buds.	.6473		Not sick		Largest dose daily 7.6 grams—25 green—0.058 pound.
No. 475	103.5	August 17	Balling gun	Dry leaves and flowers.	.160		Death	High Rolls, N. Mex	
No. 478	114	August 19	do	Dry leaves	.11		Not sick	do	
No. 490	86	August 21	do	do	.136		do	do	
No. 483	126.5	August 22	do	Dry leaves and flowers.	.138		Death	Paonia, Colo	
No. 506	120.5	August 26	do	do	.132		Not sick	do	

TABLE 1.—*Summary of feeding experiments with Asclepias galioides, 1918*—Continued.

Animal.		Date of feeding.	Method of feeding.	Part of plant used.	Weight of plant estimated as green plant for 100 pounds of animal.	Remedy used.	Result.	Where plant was obtained.	Remarks.
Designation.	Weight.								
Sheep:	*Pounds.*				*Pounds.*				
No. 478	111	August 28	Balling gun	Dry leaves and flowers.	0.138		Not sick	Paonia, Colo.	
No. 478	111	August 29	do	do	.138		do	do	
No. 478	111	September 2	do	do	.147		do	do	
No. 478	111	September 5	do	do	.167	Arecolin	Sick	do	
No. 468	96	September 7	do	do	.166		Death	do	
No. 492	111	September 11	do	do	.165	Arecolin	do	Grand Junction, Colo.	
No. 506	124	September 11	do	do	.148		Symptoms	do	
No. 506	124	September 12	do	do	.151		Not sick	Paonia, Colo.	
No. 437	108.5	September 16	do	do	.168	Atropin and morphin.	Death	do	
No. 506	124	September 16	do	do	.160		Not sick	do	
No. 506	124	September 18	do	do	.172		do	do	
No. 506	124	September 20	do	do	.184	Atropin and morphin.	Death	do	

Summary of feeding experiments with Asclepias galioides, 1919.

Animal. Designation.	Animal. Weight.	Date of feeding.	Method of feeding.	Part of plant used.	Weight of plant estimated as green plant for 100 pounds of animal.	Remedy used.	Result.	Where plant was obtained.	Remarks.
Sheep:	*Pounds.*				*Pounds.*				
No. 522	87	August 11	Balling gun	Leaves and stems	0.142		Not sick	Palisades, Colo.	
No. 522	87	August 14	do	do	.155		do	do	
No. 522	87	August 16	do	do	.162		do	do	
No. 522	87	August 18	do	do	.169		do	do	
No. 522	87	August 20	do	do	.176		do	do	
No. 521	89	August 22	do	Stems	.147		do	do	
No. 522	87	August 23	do	Leaves and stems	.183		do	do	
No. 523	93	do	do	Leaves	.147		do	do	
No. 522	87	August 25	do	Leaves and stems	.191		do	do	
No. 520	94.25	do	do	Stems	.191		do	do	
No. 526	98.5	August 26	do	Leaves	.161		do	do	
No. 522	87	August 27	do	Leaves and stems	.198		do	do	
No. 486	131.25	do	do	Stems	.206		do	do	
No. 548	109	August 28	do	Leaves	.176		do	do	
No. 522	87	August 29	do	Leaves and stems	.204		do	do	
No. 514	142.25	do	do	Stems	.220		do	do	
No. 534	108.5	August 30	do	Leaves	.191		Slightly sick	do	
No. 522	87	September 1	do	Leaves and stems	.219		Not sick	do	
No. 539	96.75	September 2	do	Stems	.250		do	do	
No. 522	87	September 3	do	Leaves and stems	.232		do	do	
No. 542	110	do	do	Leaves	.198		Symptoms	do	
No. 536	112	September 4	do	Stems	.265		Not sick	do	
No. 522	87	September 6	do	Leaves and stems	.247		do	do	
No. 518	124	do	do	Stems	.279		do	do	
No. 461	102.5	do	do	Leaves	.220	Eserin	Death	do	
No. 482	127.5	September 9	do	Stems	.294		Not sick	do	
No. 522	87	do	do	Leaves and stems	.275		do	do	
No. 372	129	September 10	do	Leaves	.206	Eserin	Sick	do	
No. 522	87	September 11	do	do	.198		Symptoms	do	
No. 556	110	September 13	do	Stems	.309		Not sick	do	
No. 486	136	September 15	do	do	.327		do	do	
No. 547	96.5	September 17	do	do	.367		do	do	
No. 541	102.5	September 19	do	do	.404		do	do	
No. 536	116.5	September 20	do	do	.367		do	Rockville, Utah	

Summary of feeding experiments with Asclepias galioides, 1919—Continued.

Animal.		Date of feeding.	Method of feeding.	Part of plant used.	Weight of plant estimated as green plant for 100 pounds of animal.	Remedy used.	Result.	Where plant was obtained.	Remarks.
Designation.	Weight.								
Sheep—Con.	*Pounds.*				*Pounds.*				
No. 522	86	September 22	Balling gun	Leaves	0.147		Somewhat sick.	Rockville, Utah	
No. 534	112.5	do	do	Stems	.404		Not sick	do	
No. 544	98.75	September 25	do	do	.477		do	do	
Horse:									
No. 126	1,030	August 20 to 25	Fed in hay	Leaves and stems			do	Palisades, Colo.,	Ate only a small quantity.
No. 126	1,050	September 15	do	Leaves	.161		Death	Rockville, Utah	

HORSE EXPERIMENTS.

Only one horse, No. 126, a 5-year-old gelding weighing 1,020 pounds and in fine condition, was used for experimental feeding. At 3.36 p. m. July 30, 1918, the animal was given 1,020 grams, equal to 0.22 pound per hundred weight of animal, of *Asclepias galioides* which had been shipped from Hotchkiss, Colo. The plant was mixed with 5 pounds of alfalfa hay. The feeding was entirely eaten by 5.15 p. m. of the same day. The horse was kept under observation until 10.30 p. m. and during that time no symptoms appeared. It was seen again the following morning, July 31 at 7.45 a. m., when it seemed slightly paralyzed in its hind legs and while being driven from one pen to another, fell down. At 8 a. m., its pupils were dilated and it was moving uncertainly about the corrals, evidently not having entire control of its legs. When hurried it fell. At 8.30 a. m. it was staggering about the corral; would walk a few steps, tremble, spread its legs apart and fall. As it went down its head was bent toward its breast and its lips were drawn back from its teeth. It perspired freely and the pupils were dilated. These motions were repeated again and again. The animal rose from the reclining posture with difficulty and in its attempt to move about the corral was uncertain in its movements and staggered from side to side. It could stand for only an extremely short time and then would fall and again attempt to rise.

Plate V, figures 1, 2, 3, 4, 5, and 6, show its attitude at various times between 8.25 and 8.45 a. m. Figure 1 shows the attitude assumed during the spasms. The head is extended rather rigidly and the legs drawn close to the body. In figure 2 the animal is shown in a brief period of rest before attempting to rise. Figure 3 shows the characteristic staggering as it attempted to move about the corral. In figure 4 its head is drawn close to the breast, an attitude frequently assumed in the spasms. In figure 5 the horse is attempting to rise. It was noticed in these attempts that it had less control of the hind legs than of the fore legs. These motions were repeated every 2 to 5 minutes and it was noticed that in falling the animal almost invariably fell upon its right side, the head sometimes striking the ground with great violence. Figure 6 shows the animal just as it is attempting to raise its head from the ground.

Plate VA, figure 1, taken at 8.57 a. m., shows the horse in one of its attitudes when attempting to stand. As stated, the animal would fall upon its right side and roll upon its belly and then attempt, with greater or less success, to rise. During this time it breathed with forcible expirations, frequently accompanied with grunts. Figure 2 of the same plate shows the animal again in one of its attempts to get upon its feet. These motions were repeated frequently, the animal being unable to get upon its feet between about 9 o'clock and 11.30 a. m. Figure 3, taken at 10.30 a. m., shows the horse in the midst of one of its spasms. Figure 4, taken at 11.24 a. m., shows a very characteristic attitude in which the horse draws its head back, baring its teeth. Generally speaking, in the spasms the head was drawn back in the position of opisthotonos, or the head was drawn close to the breast. The animal was not quiet more than 5 or 10 minutes at any time. At 11.39 a. m., it got upon its feet, moved a short distance, and then fell again. This was repeated a number of times before 12 o'clock and at 12.17 it was again able to get upon its feet and staggered across the corral, but immediately fell, going down with considerable violence. This was repeated two or three times before 1 o'clock p. m. Figure 5, taken at 1.03 p. m., shows the animal in one of these brief intervals when he was upon his feet. At 1.35 p. m. it was noticed that the walking movements, which were seen very markedly in sheep, were noticeable and later became more rapid, so that between 2 and 3 o'clock the movements of the legs were much like those made by an animal in running. During this time the animal, when down, was always on its right side and moved its head back and forth upon the ground with such violence as to result eventually in the loss of sight in the right eye.

The condition of the horse remained practically the same through the remainder of the afternoon and evening. The last observation was made at 10.45 p. m. At 2.30, 3.10, and 4.40 one grain of arecolin was given subcutaneously. It was noticed at the last observation in the evening that it would attempt to eat hay which was placed before it. The first observation on August 1 was at 7.15 a. m., and at that time the horse was in practically the same position as when left the night before. When disturbed it rolled upon its belly, but had great difficulty in maintaining that position. At 7.25 it was found standing, being especially weak in the hind legs. At 8 o'clock it walked into the next corral and drank water copiously.

Plate Va, figure 6, taken at 8.45, shows the general attitude of the animal when standing. It continued to improve and remained on its feet during the day, gradually reaching almost complete recovery. It was noticed, however, that at different times, a month later, when he was being driven, he would suddenly fall with considerable violence. It was thought at the time that these falls were partly due to defective eyesight, as he was practically blind in the right eye. As it is possible that a permanent systemic injury was produced by the Asclepias poisoning, the animal was kept under observation another year. Whether the arecolin had any marked effect in aiding in recovery is a matter of doubt. It is a fact, however, that the animal was very sick, and the experience with other animals shows that most cases end fatally. It is possible, therefore, that the arecolin had some value. This horse was fed *Asclepias galioides* again on September 20, and received 0.14 pound per hundredweight of animal. This was given at 2.05 p. m., and the animal was kept under observation during that and the three succeeding days, but showed no symptoms during that time.

In the fall the horse was taken from the station to a pasture near Salina, where it was kept during the winter. It was reported by the forest ranger who drove the animals down that No. 126 whirled around a number of times, drew its head down and fell, but soon got up and went along. It was also reported that it acted queerly at various times during the winter. It was driven to the station again May 28, 1919, when it was in very good condition. During June and the first half of July, it was repeatedly observed to stop suddenly, whirl about one or more times, draw the head toward the breast, and fall. These fits seemed to come suddenly when the animal was running or excited. In the latter part of July it was fed another species of Asclepias with no effect, and from August 20 to 25 an attempt was made to have it eat *Asclepias galioides*, but with no success.

On September 15, 1919, within about 7 hours, it ate 0.507 pound of dry *Asclepias galioides*, which is equivalent to 0.161 pound of green plant per hundredweight of animal. The material fed consisted of leaves only and was mixed with chopped alfalfa. As shown elsewhere (p. 37) it has been found that the leaves of *Asclepias galioides* are much more toxic than the stems, so that this quantity, 0.161 pound, was really a much heavier dose than that of the preceding year, 0.22 pound, which consisted of stems as well as leaves. The feeding was given at 10.50 a. m. and the above-mentioned amount had been consumed at 5.23 p. m. At that time there were symptoms of intoxication, weakness in the hind legs being especially noticeable. These symptoms gradually became more pronounced until at 7.13 the animal went into a spasm. After that the spasms followed one another at exceedingly short intervals and it exhibited all the symptoms seen in its case the preceding year. It was kept under constant observation until death, which occurred at 12.28 p. m., September 16.

The autopsy was made immediately after death. The stomach was greatly distended with gas, and parts of the wall were deeply congested. There were congested areas in the jejunum, ileum, and cecum. The spleen and pancreas exhibited some congestion. The brain and spinal cord were congested, there were areas of hemorrhage between the medulla and cerebrum, and minute hemorrhagic areas on the surface of the cord. The heart was in diastole; it was unusually large and the walls were flabby.

CATTLE EXPERIMENTS.

Two head of cattle were used in the feeding experiments. No. 815 was fed four times; August 1 it received 0.163 pound of *Asclepias* *galioides* per hundredweight of animal; August 8, 0.22 pound; August 13, 0.242 pound, and August 17, 0.294 pound. None of these feedings took effect.

No. 750 also was fed four times. It was a steer that was locoed in 1917, but under continued treatment was practically cured, although not quite in full flesh. The animal would be considered in fair condition. On August 22 this animal received 0.22 pound per hundredweight of animal, which produced no effect. On August 25 it received 0.626 pound per hundredweight of animal, again with no result. In the feeding of August 22 the material was eaten within 4 hours; in the feeding of August 25 it was eaten in about 2½ hours. On August 26 the animal received 0.848 pound per hundredweight of animal, but unfortunately no note was made as to whether all was consumed. No symptoms appeared during the day. On the next day, however, August 27, at 9.13 a. m., it was noticed that the muscles of the fore legs and the neck were quivering in an abnormal manner.

At 12.01 noon the animal fell upon its stomach, throwing the head back and kicking spasmodically with its fore legs. It then lay upon its belly with the forefeet doubled under the thorax and hind legs stretched out, in a position as shown in Plate VI, figure 2. Figure 1 shows the animal just before it fell. It then got up and moved about, staggering and trembling, with its hind legs far apart. At 12.10 it was found moving in an unsteady way with shoulders twitching violently and breathing with grunts. Saliva was dripping from its mouth. Figure 3 shows the attitude at that time. It moved about in a weak way, sometimes turning toward the right, and soon went down again. Figures 4, 5, and 6 show the attitudes which it assumed while attempting to stand. At 12.35 it went down, pushing forward with great violence. Plate VIa, figure 1, shows its attitude as it came down upon the ground. It turned over upon its left side, then back upon its belly with the hind legs extended, but at 12.37 it was again on its feet. Figure 2 shows the animal on its feet again at 12.40. Figure 3 shows how it attempted to move rapidly and had difficulty in maintaining itself. At 12.44 (fig. 4) it started to run and went against the wall of the corral, fell down upon the right side with legs stiffly extended, but rose in a few seconds, and at 12.45 was down again, but at 12.46 was on its feet. At 12.50 it fell, rolled over on its stomach, and then dragged itself along, in its attempts to rise. This position is shown very clearly in figure 5. Figure 6 shows its position at 12.52 p. m. These movements were repeated again and again. It ordinarily remained on its feet not more than 10 or 15 minutes at a time.

At 1.35 p. m., however, the animal seemed quite strong and when made to run around the corral for two or three minutes did not fall, although it still staggered. At 1.57 after being run about it ran into

FIG. 1.—ASCLEPIAS GALIOIDES GROWING IN AN ABANDONED ORCHARD.

FIG. 2.—A YOUNG PLANT OF ASCLEPIAS GALIOIDES GROWING FROM A PIECE OF ROOT ABOUT ONE-FOURTH INCH LONG.

FIG. 1.—Horse 126 at 8.25 a. m., July 31, in a spasm.

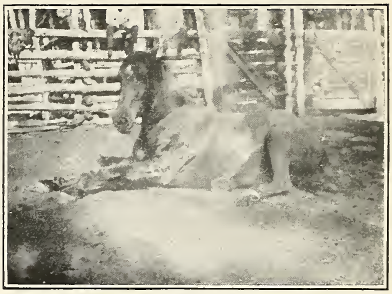

FIG. 2.—Horse 126 at 8.30 a. m., July 31.

FIG. 3.—Horse 126 at 8.32 a. m., July 31, attempting to stand.

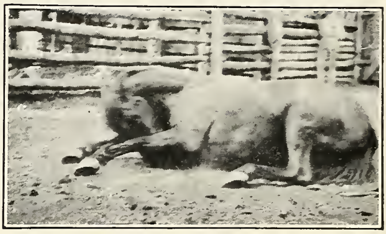

FIG. 4.—Horse 126 at 8.45 a. m., July 31, showing the position with head drawn to the breast.

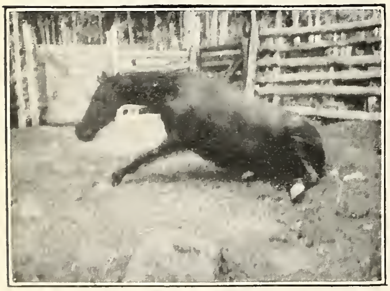

FIG. 5.—Horse 126 at 8.45 a. m., July 31, attempting to rise.

FIG. 6.—Horse 126 at 8.54 a. m., July 31, attempting to recover from a prostrate position.

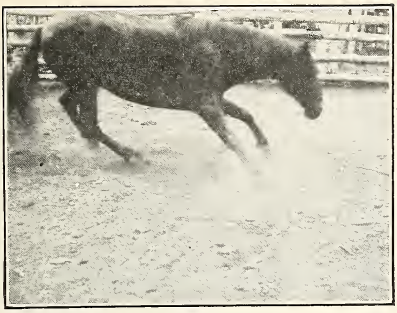

FIG. 1.—Horse 126 at 8.57 a. m., July 31.

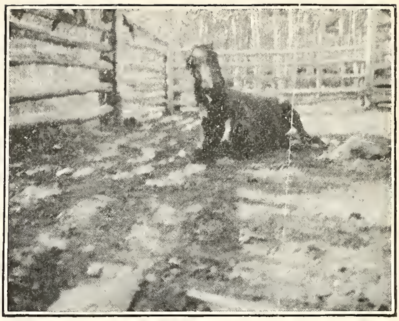

FIG. 2.—Horse 126 at 9.42 a. m., July 31.

FIG. 3.—Horse 126 at 10.30 a. m., July 31.

FIG. 4.—Horse 126 at 11.24 a. m., July 31.

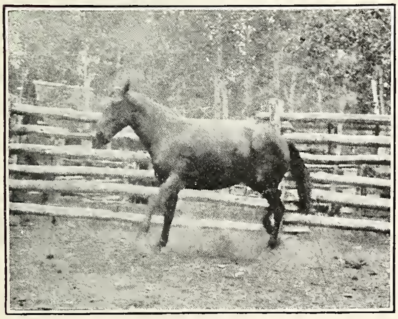

FIG. 5.—Horse 126 at 1.03 p. m., July 31, when able to get upon his feet for a minute or two.

FIG. 6.—Horse 126 at 8.45 a. m., August 1, when improved sufficiently to remain upon his feet.

FIG. 1.—Steer 750 at noon.

FIG. 2.—Steer 750 at 12.01 p. m., showing its position after falling.

FIG. 3.—Steer 750 at 12.10 p. m., when moving unsteadily.

FIG. 4.—Steer 750 at 12.12 p. m.

FIG. 5.—Steer 750 at 12.14 p. m.

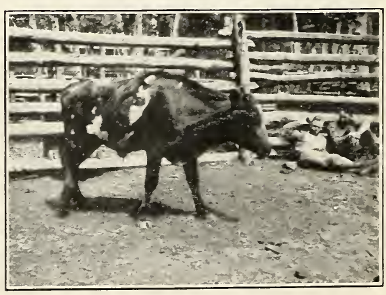

FIG. 6.—Steer 750 at 12.34 p. m.

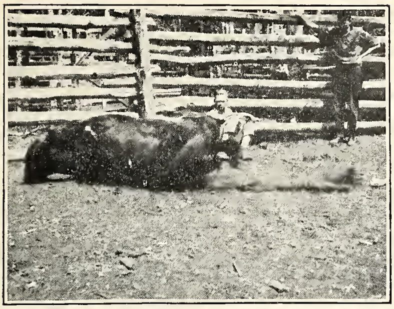

FIG. 1.—Steer 750 at 12.35 p. m., after falling forward.

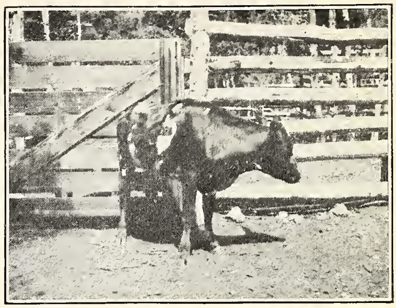

FIG. 2.—Steer 750 at 12.40 p. m., when upon its feet again.

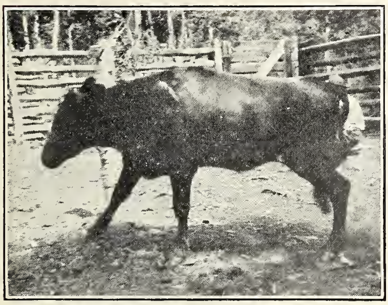

FIG. 3.—Steer 750 at 12.43 p. m., when staggering.

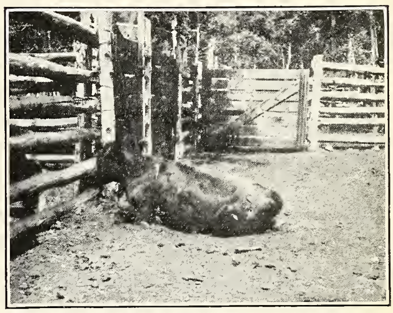

FIG. 4.—Steer 750 at 12.44 p. m., after falling.

FIG. 5.—Steer 750 at 12.50 p. m., dragging itself along after falling.

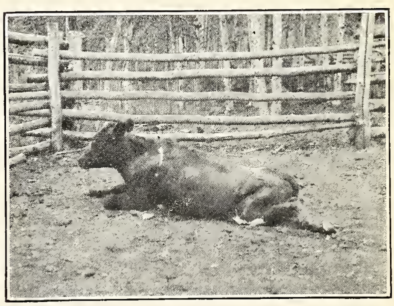

FIG. 6.—Steer 750 at 12.52 p. m.

the wall of the corral and fell. This was repeated two or three times, and it was noticed that before falling the head was drawn toward the body in somewhat the same attitude as that assumed by Horse 126. After 2 p. m. the steer was considered on the road to recovery and was able to remain upon its feet. It was kept in the corral until 5.30, August 28, when it was turned into the pasture. At that time, while it had recovered, it seemed somewhat weak and staggered when driven. Thereafter its recovery seemed to be complete.

On September 22, at 10.45 a. m., it was given 450 grams of dried plant, which was equivalent to 0.551 pound of green plant per hundredweight of animal. This animal was fed with about 5 pounds of alfalfa hay, and it was expected that this quantity might be sufficient to produce fatal results. By noon all but 2 pounds of the mixture had been eaten, and while no note was made of the completion of the feeding, it is supposed that the remainder was eaten during the afternoon.

At 7.15 a. m., September 23, the animal was found lying on the right side, and evidently had been lying and kicking for a considerable period. An unusual noise was heard in the corral that morning at 3.45 but was not investigated and it was presumed that the animal was down at that time. The pupils were dilated and the jaw moved constantly as if it were chewing. From that time until death, at 3.35 p. m., the animal was upon the ground most of the time and there were almost continuous spasms. It was considerably bloated and frequently breathed with groans. Considerable gas was belched from the stomach, which may have relieved the bloating to some extent. During the spasms the pupils were dilated and it was evident that the animal had salivated considerably.

Sometimes it bellowed loudly as though in pain and most of the time the spasms were so frequent that the motion of the legs was nearly continuous in a walking or running movement. In the spasms the head was sometimes drawn back in the position of opisthotonos, while at others it was drawn to the breast. This condition continued until death.

Immediately after death an autopsy was made. The body was considerably bloated, the gas being especially evident in the first and second stomachs. The blood vessels of the ileum were unusually full. The only other abnormal condition was the fullness of the blood vessels in the meninges of the brain and of the spinal cord.

SHEEP EXPERIMENTS.

Twenty-nine different experiments were made with sheep during the season of 1918. Of these 2 were sick and recovered and 10 died. Thirty-seven experiments with sheep were made in 1919. Of these 4 exhibited symptoms, 4 were sick, and 3 died. A general summary of these cases is given in Table 1. In three of the experiments the plant, mixed with hay, was fed to the animals. In all other cases the feeding was by the balling gun, so that the animals received the material in a very short time. It does not seem necessary to give the details of all these cases, as they were very simple. Two cases that were fairly typical have been selected for an extended account.

Sheep 478.

This animal was an old ewe, in fair condition, weighing 100.5 pounds. On June 19 at 10.30 a. m. its temperature was 102.8° F., pulse 108, and respiration 39. Between 10.38 and 10.40 a. m. it was given, with the balling gun, for each hundredweight of animal, 0.165 pound of *Asclepias galioides* from Hotchkiss, Colo. The animal was kept under observation during that and succeeding days and showed no symptoms of poisoning. The highest temperature reached was 103.4° F., at 11 a. m. June 19. The animal, then weighing 114 pounds, was brought in August 19, 1918, for another experiment with the plant. At 10.03 a. m. its temperature was 102.1° F., its pulse 90, and respiration 48. At 11.09 it was given, for each hundredweight of animal, 0.11 pound of green *Asclepias galioides* which had been collected near High Rolls, N. Mex. There was no result from this feeding.

On August 28, when the animal weighed 111 pounds, another experiment was made. At 9.50 a. m. its temperature was 100.9° F., pulse 60, and respiration 36. At 11.35 a. m., for each hundredweight of animal it was given 0.138 pound of green plant of *Asclepias galioides* which had been collected near Paonia, Colo. From this feeding there was no result. On the next day, August 29, at 10.23 a. m., for each hundredweight of animal 0.138 pound of green plant of *Asclepias galioides* was given. This experiment, too, was without effect. On September 2 it was given 0.147 pound of green plant per hundredweight of animal, again without effect. On September 5 at 2.30 p. m. it received 0.167 pound of green plant per hundredweight of animal, the material having been collected near Paonia, Colo. The animal was kept under observation and no symptoms were noticed until 11.35 a. m. September 6. At that time it went down on its knees and lay stretched out upon the stomach. A subcutaneous injection of one-fourth grain of arecolin was given at 11.57. At 11.59 it was attempting to get up, but was unable to do so. The head was thrown back in the position of opisthotonos and then at times drawn to the breast. The respiration was labored.

Plate VII, figure 1, shows the attitude assumed by the animal at 11.57 and figure 2 at 11.58. Figure 2 is a characteristic attitude when the animal was kicking about, with its head thrown far back. At 12.02 p. m. the sheep was placed upon its feet but was unable to

FIG. 1.—Sheep 478 at 11.57 a. m.

FIG. 2.—Sheep 478 at 11.58 a. m. A characteristic attitude when in a spasm.

FIG. 3.—Sheep 478 at 12.24 p. m., when attempting to rise.

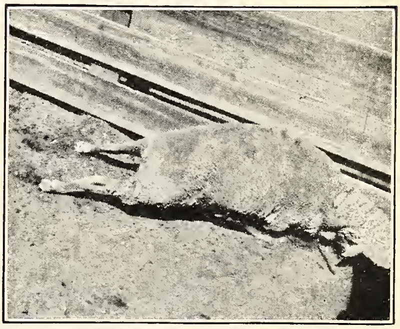

FIG. 4.—Sheep 478 at 12.41 p. m., after falling forward.

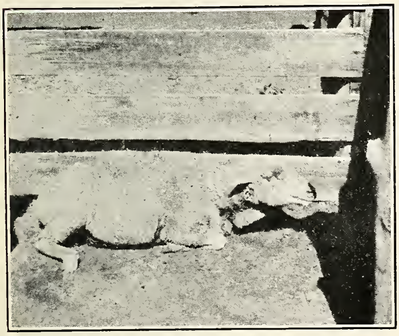

FIG. 5.—Sheep 478 at 12.45 p. m., in one of the intervals between spasms.

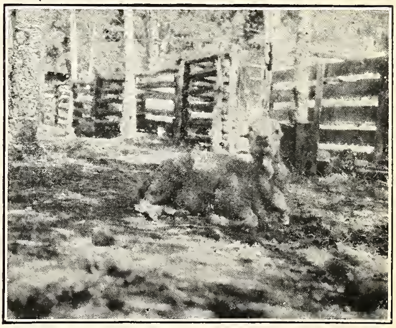

FIG. 6.—Sheep 478 at 1.05 p. m., when recovering.

stand. The respiration continued deep and labored. At 12.14 it got upon its feet, ran across the pen and fell down. This was repeated two or three times. At 12.25 it was able to stand for a few seconds, but fell forward again. At 12.31 it got up, fell twice, then got upon its feet and fell forward across the pen. Figure 3, taken at 12.24 p. m., shows its attitude when attempting to rise. Figure 4, taken at 12.41 p. m., shows the attitude as it fell forward in crossing the pen. Figure 5, taken at 12.45 p. m., shows the attitude when lying more quietly. At 12.45 p. m., it was given another dose of one-fourth grain of arecolin. In the spasms the eyes were dilated. and the head was either drawn to the breast or thrown far back. At 1 p. m. the animal seemed somewhat stronger, and it was taken out of the pen. It was then able to hold its head erect. Figure 6 shows the attitude assumed by the animal. After this the spasms were less frequent and it seemed to be gaining in strength. At 2.14 p. m. it was able to walk about 25 feet and a little later seemed to walk quite normally. It continued to gain in strength until about 4.40 p. m., when the condition seemed fairly normal. From that time it gained steadily.

The temperature was taken at intervals during this illness. At 6.35 p. m., September 5, it was 102.2° F., at 10.08 a. m., September 6, 100.2°, at 12.06 p. m., 103.7°, at 12.25, 104.4°, at 6.19 p. m., 103.3°, and the next morning, September 7, at 8.13 a. m., 100.9° F.

Sheep 476.

Sheep 476 was an old ewe, weighing 81.5 pounds at the time of experiment. On June 20 at 12.22 p. m. it was given 0.27 pound of *Asclepias galioides* per hundred pounds of animal. This was given by the balling gun, and the feeding was finished in about three minutes. The temperature at 2.20 p. m. was 101.9° F., pulse 102, and respiration 30. At 3.45 the temperature was 102.6°, pulse 150, and respiration 24. The respirations were deep and labored but regular. The sheep was down on its side with the head thrown back, and immediately went into a series of spasms. The legs were extended and stiff. At 3.55 p. m., while lying up its side, it was moving the legs as if running. The respiration was labored and the expiration forced. The heart was beating nearly 200 times a minute. The movements of the legs at times were slow and at other times very rapid. At 4.07 p. m. there was frothing at the mouth, bloating, and some gas was belched. These actions were repeated every 2 to 5 minutes during the afternoon. The bloating was very marked. At times the animal was trembling. In the spasms the head was drawn back and brought to the breast, and during that time the temperature went up to 105° F. The respiration was never rapid and was labored during the full period. The spasms were repeated with very great frequency between 6.57 p. m. and 7.17 p. m. A record of the number of the spasms was taken and it was found that 59 occurred during the period. At 7.20 p. m. there was a violent spasm. The animal straightened out its legs, the heart stopped beating, and gas bubbled up through the throat and mouth.

In the autopsy upon this animal very little was noticed that was abnormal; in fact, this autopsy should hardly be considered typical. In the summarized account of the autopsies on page 28 is given a statement in regard to the general appearances of the internal organs of the animal after death.

CHEMICAL EXAMINATION.

No analysis of *Asclepias galioides* appears to have been made before this investigation and, although the present chemical examination has not been completed, it appears to be desirable to record the definite results already obtained.

The plant material used for the chemical work was taken from the same stock lots as that used in the feeding experiments and was consequently identical with it. Most of it was carefully dried and ground in a drug mill. One portion of green plant was, however, examined, but was found to contain nothing of a toxic nature which is not present also in the dried plant.

No attempt was made to determine all the constituents of the plant by a routine phytochemical analysis, since for this investigation, the substances responsible for range poisoning were alone important. On that account the chemical procedure was conducted primarily to yield knowledge of them.

A portion of the dried plant was extracted with petroleum ether and the extract was found to contain a large quantity of caoutchouc with coumarin and fatty matters. Several portions were exhausted with alcohol, which removed all the toxic substances. This extract was partly soluble in water and both the solution and the residue were toxic. The aqueous solution contained a very small quantity of a nontoxic alkaloidal substance corresponding to less than 0.01 per cent of the weight of the dry plant, two glucosids which may be separated from each other by their different solubility in chloroform, and sugars which appear to consist of maltose and a sugar which yields dextrosazone. Both of the glucosids are toxic and produce narcosis.

The water-insoluble portion of the alcohol extract contains fats, an orange-red coloring matter, a phytosterol, nontoxic resin acids, toxic glucosids which are probably identical with those found in the water-soluble fraction, and the substance which causes the spasmodic symptoms observed in animals. After a complicated manipulation the last substance was obtained as a colorless, brittle, resinous mass which has not yet yielded anything of a crystalline nature. It melts indefinitely at about 60° C., is insoluble in water, aqueous acids, and alkalies, is very soluble in alcohol, amyl alcohol, glacial acetic acid, acetone, chloroform, ether, benzol, acetic ether, and pyridine. It does not appear to be glucosidal. Further investigation, with the object of determining its precise chemical nature, is in progress.

This substance has been thoroughly tested upon guinea pigs and produces the characteristic symptoms observed on the range, with the typical lesions.

Fresh samples of the plant were tested for the presence of volatile poisons and toxic saponins, with negative results.

PHARMACOLOGICAL RESULTS.

The pharmacological work was conducted according to the following plan: Each of the various fractions resulting from the chemical treatment of the plant extracts was administered through the mouth to an animal. Extracts which contained much matter insoluble in water were emulsified in that liquid with either acacia or mucilage of Irish moss; soluble extracts were given in water solution. Frequent control animals served to exclude accident.

The animals used were sheep and guinea pigs. The larger proportion of the testing was done with the latter animals, which were found to react excellently and characteristically to the toxins of the plant, duplicating the symptoms observed in the experimental sheep almost to the most minute detail. In indefinite cases the tests were repeated upon several animals; 126 experiments in all were conducted. As criteria in the work upon the guinea pigs were taken the symptoms and pathological lesions exhibited by the experimental sheep. By following this plan it was found possible to exclude many of the plant constituents as innocuous or as not factors in range poisoning and to locate definitely the fractions which contain toxic substances.

Three general and distinct types of intoxication were observed in guinea pigs which were drenched with toxic fractions of extracts from this plant.

The first type closely resembles the typical cases of range poisoning which follow the ingestion of the whole plant. This type of intoxication is produced by the resinous substance described above; it commences with a general weakness, the animal appears disinclined to move about, and is soon narcotized. After an interval convulsions appear, with the characteristic running movements in many cases and the peculiar tendency to fall and lie always on the same side of the body. Clonic spasms, often with the typical drawing of the head to the thorax, are observed some time after the general convulsions have commenced. When resting between spasms the animal usually lies stretched out with the head in opisthotonos. All the animals which exhibited spasms eventually died. The autopsy showed, in general, heart in diastole with surface vessels full, lungs normal, liver, spleen, and kidneys usually normal, digestive tract normal, often containing much gas, central nervous system congested. This is similar to the typical picture in cases of range poisoning.

A second general type of cases is produced by the glucosid that was isolated from the water-soluble fraction of the alcohol extract by chloroform after making the solution alkaline. This type of case is not observed on the range because the quantity of the causative agent contained in a toxic dose of the plant is too small to assert itself over the spasmodic substance. Animals drenched with solutions of this glucosid are completely narcotized within a few minutes of the administration of the dose; they fall upon the side and are indifferent to stimuli. The respiration is deep and regular and the heart beat is normal. Animals remain in this condition for several hours and finally die with symptoms of respiratory paralysis. On autopsy these animals frequently show congestion of the digestive tract and of the central nervous system, but in some cases the brain and cord appeared normal.

The third general type of poisoning is produced by the glucosid which is not extracted from the aqueous solution of the alcoholic extract by chloroform. In these cases the animal shows no marked symptoms for several hours after the administration of the dose. Then there is evidence of weakness which continues, the animal loses weight rapidly, finally goes down upon the belly with the legs sprawled out, and dies in from 5 to 7 days after the drench. The autopsy in these cases does not furnish typical lesions; usually all the organs appear normal, but occasionally there is fullness in the central nervous system. Range cases do not show this type of intoxication for the same reason adduced in the case of the second type.

EXPERIMENTAL.

The following account of some typical experiments furnishes an indication of the general methods employed in the chemical investigation, leaving the more extended and detailed description for future publication.

Moisture, ash, and extract determination.—The material used for these determinations was dried *Asclepias galioides* collected in July, 1918, at Paonia, Colo., and reduced to a No. 60 powder.

	Per cent.
Moisture	6.22
Ash	11.38

Fifty grams were extracted in a Soxhlet apparatus with various solvents in succession:

	Grams.	Per cent.
Petroleum ether extracted	2.461	4.92
Benzol	1.293	2.58
Ether	0.274	0.54
Chloroform	0.636	1.27
Acetone	1.369	2.73
Alcohol	5.460	10.92
Total	-----	22.96

Each of these fractions was tested upon guinea pigs. The petroleum ether, acetone, and alcohol extracts were nontoxic; the benzol fraction produced the characteristic spasmodic type of intoxication observed on the range, and the autopsy exhibited the typical pathologic picture. The chloroform and ether extracts were toxic, producing narcosis.

Alkaloids.—Twenty-five grams of fresh plant were cut into small pieces and macerated for 24 hours in excess of 1 per cent hydrochloric acid. The yellowish extract, after filtration, reacted with the ordinary alkaloidal reagents, giving evidence of a minute quantity of basic substance. The base was not precipitated from its aqueous solutions by potassium hydroxid or ammonia.

Volatile poisons.—A total of 912 grams of the dried leaves and blossoms of *Asclepias galioides* collected at Paonia, Colo., in July, 1918, was mixed with 45 grams of barium hydroxid and 15 liters of water and allowed to stand overnight. The following morning the solution was tested and found to be alkaline to litmus. The mass was then distilled. This irregular procedure was necessary because the experiment was made in the field under conditions which did not permit of the most refined manipulation. There were obtained 2,400 mils of distillate, with an odor of tea. This was not alkaline and gave no pricipitate with Mayer's solution in the presence of hydrochloric acid. On standing, a minute quantity of oil collected on the surface. One thousand two hundred mils of this distillate, representing the volatile constituents of 456 grams of dried leaves and blossoms, were drenched into Sheep 491, weighing 130 pounds, without producing any effect.

Saponins.—Four hundred grams (about 20 toxic doses) of dried and ground Asclepias from Hotchkiss, Colo., were mixed with 4 liters of alcohol, allowed to stand 24 hours, and heated to boiling. The mass was maintained at the boiling temperature for an hour and then was filtered hot. The filtrate was a bright, full green. On cooling and standing, a small quantity of green waxy material separated, which was collected on a filter and washed with alcohol. It was insoluble in water and cold alcohol, was completely soluble in chloroform, and gave no reaction with ferric chlorid. Two half-gram portions of it were suspended in water and drenched into a guinea pig without effect.

Alcohol extract.—Four thousand three hundred grams of the dried whole plant were extracted with alcohol, the solvent removed, and the residue treated with hot water, which dissolved a large quantity of it and left a resinous mass undissolved. Both the water solution and the residue were toxic; the solution produced a peculiar narcosis and the resin caused the characteristic spasmodic symptoms observed in range poisoning.

The resin.—This was divided into 4 fractions by treatment with petroleum ether, benzol, and alcohol in succession, when a small residue remained which was insoluble in the ordinary organic solvents, but dissolved in dilute sodium-carbonate solution and was nontoxic. The petroleum-ether fraction was nontoxic; the benzol fraction produced the spasmodic type of intoxication; the alcohol fraction was narcotic.

The aqueous solution.—A portion of this solution was investigated for the presence of toxic saponins, by treatment with barium hydroxid, and testing the various fractions obtained on guinea pigs. Nothing in the nature of a saponin was detected.

The main portion was made alkaline and extracted with chloroform. This treatment yielded a small quantity of a nontoxic alkaloid and a glucosidal substance which has strong narcotic properties. The aqueous liquid which remained after the chloroform extraction was still toxic, producing narcosis in experimental animals, and from it a second toxic glucosidal substance has been isolated.

The marc.—The marc remaining after the alcohol percolation was then extracted with boiling alcohol and this extract was kept separate from the first. The marc remaining after this treatment was thoroughly dried to free it from alcohol and tested for toxicity. On August 2, 1918, 43.5 grams of marc (60 grams of dried plant) were forced fed to Sheep 479, weight 93 pounds. This feeding produced no apparent effect, and on August 4 the same sheep received 87 grams of the dried marc, also without effect. On August 6 a further quantity of 174 grams of marc were forced fed to the same sheep, again without effect. On August 7, 269 grams of the marc were forced fed to Sheep 497, weight 81.5 pounds, and produced no effect. The marc evidently did not contain toxic matter responsible for the cases observed on the range.

SUMMARY OF CHEMICAL EXAMINATION.

The plant material used was identical with that employed in the feeding experiments. The fresh green plant and the dried plant were examined and the fractions into which the extracts were divided were tested for pharmacological activity.

The investigation has yielded the following preliminary results: *Asclepias galioides* appears to contain several toxic compounds, some of which are glucosidal in nature. The substance which is responsible for the symptoms observed in range poisoning may be extracted from the plant with cold alcohol and is insoluble in hot or cold water. The plant yields water-soluble toxins, probably glucosids, which cause narcosis in experimental animals without congestion of the central nervous system.

In addition, the plant contains less than 0.01 per cent of an alkaloid which does not appear to be toxic and certainly does not influence the range cases. Attempts to discover toxic saponins in the plant were unsuccessful.

PART III.—GENERAL DISCUSSION AND CONCLUSIONS.

SYMPTOMS.

Generally speaking, the first evidence of intoxication is the loss of control of the muscles. The animal staggers when walking and eventually falls and is unable to rise. Sometimes it is found down before any other symptons appear. At this time there is, in most cases, salivation and there may be marked trembling.

The horse was in profuse perspiration. The loss of muscular control is most marked in the posterior part of the animal. The period during which the animal can remain upon its feet is generally very short. When down it generally makes strenuous efforts to rise but falls back with a good deal of violence. This feature was very marked in the case of the horse. It may be noted that in the range cases the animals are said to knock their heads on the ground. Soon there commences a series of clonic spasms. It is shown by the autopsies that the stomachs are greatly distended with gas, which is also true, to some extent, of the intestines. The formation of the gas continues during the period of intoxication, with some relief by belching and the spasms are correlated with the gas formation.

The bloat caused by the gas was one of the most noticeable features in the poisoned sheep. Vomiting occurred in one case, but was not a usual symptom. In the spasms the pupils are widely dilated. The spasms may become more or less tetanic in character. Ordinarily the animal throws itself repeatedly into a position of opisthotonos, as shown in Plate VII, figures 2 and 3, and this may be followed by a position close to emprosthotonos. Very characteristic is the position shown in Plate V, figures 1 and 4, in which the chin is brought down to the breast in a tetanic spasm. This was shown with especial clearness in Horse 126. Generally in this position the feet were drawn up to the body as shown in Plate V, figure 1. The spasms are sometimes very violent and apparently accompanied with a good deal of pain. When attempting to rise the animal repeatedly falls, and, because of the inability to raise its head from the ground frequently ruins the sight of the eye on the under side as its head is moved back and forth. It sometimes groans, and the respiration is commonly labored, with forced expiration. The pulse is rapid and weak, but the respiration is not much faster than normal; the spasms are frequently accompanied with convulsive movements of the jaw.

No series of temperatures were taken in the cases of the horse and steer. Several series were taken of the sheep and with fairly uniform results. Generally speaking there was a marked elevation in temperature soon after the first symptoms appeared. In some cases this high temperature appears for only a very short time, while in others,

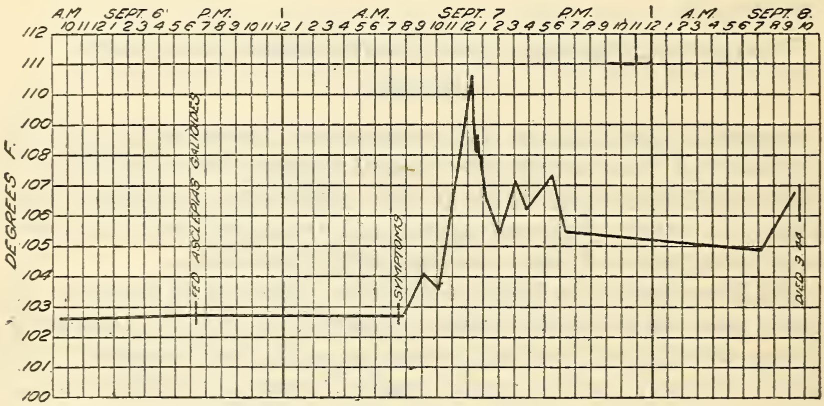

FIG. 2.—Temperature curve of Sheep 461.

as in Sheep 492, it continues for several hours. In all cases it becomes lower before death. Figure 2 shows the curve of temperature in Sheep 461, figure 3 in Sheep 483, and figure 4 in Sheep 492. In Sheep 461 it ran up to 110.6° F., the highest temperature observed. The increase in temperature, however, was not so marked in all cases. In Sheep 506 it reached only 103.4° F., but in the case of this animal it was distinctly an increase, and as the case continued during the night observations were dropped. A more complete set of observations might have shown more rise in temperature.

Glover, Newsom, and Robbins report the temperature of one of their experimental sheep in which a maximum of 110° F. was reached.

As the illness proceeds, in the intervals between the spasms, while lying upon its side, the animal moves its legs as though walking; these movements may become very rapid, as though the animal were running. These "running" movements are distinctly characteristic of the milkweed poisoning. There may be intervals of coma, but more commonly the spasms continue until death. Generally the spasms occur at short intervals and there may be as many as 4 or 5 in a minute. They become somewhat reduced in intensity toward the end. Death comes from respiratory paralysis.

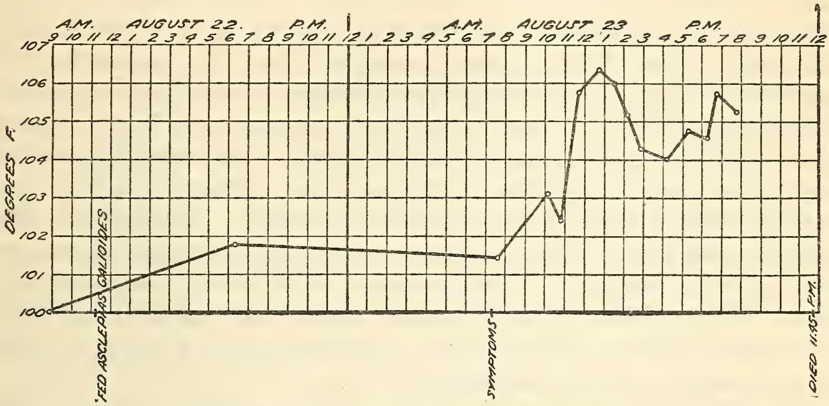

FIG. 3.—Temperature curve of Sheep 483.

The symptoms may be considered as falling into four more or less clearly marked stages:

1. A period of partial paralysis with staggering movements and falling.

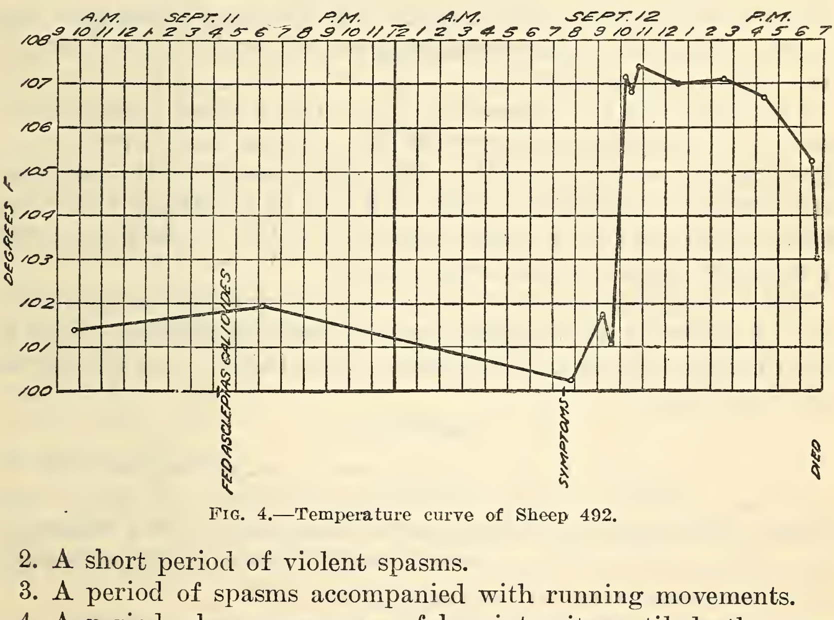

FIG. 4.—Temperature curve of Sheep 492.

2. A short period of violent spasms.

3. A period of spasms accompanied with running movements.

4. A period when spasms are of less intensity until death comes by respiratory paralysis.

AUTOPSY FINDINGS.

As noted in the description of symptoms, bloating is noticeable in practically all cases. This is found to be the result of the accumulation of gas not only in the first stomach, as is usual in most cases of bloating, but also in other parts of the alimentary canal. In the steer, No. 750, the gas occurred only in the first and second stomachs. Five of the 11 sheep autopsied had all 4 stomachs distended with gas. In one the gas was confined to the first and second stomachs and in 2 it was in the first, second, and fourth. In 3 there were no marked accumulations of gas in any of the stomachs, but the animals were bloated during their illness and the gas largely escaped either before death or soon after. In one case, 483, the gas was found in the duodenum, jejunum, ileum, and cecum, as well as in the stomachs. The distension of the cecum was noted in 6 cases. The presence of an abnormal quantity of gas in the alimentary canal may be considered as a condition always present in cases of poisoning by *Asclepias galioides.*

More or less congestion was found in the walls of the fourth stomach, duodenum, jejunum, ileum, and cecum. The colon was congested in only one case, No. 506, in which there was congestion in the second and third stomachs, as well as the fourth.

The lungs were congested in 5 of the 11 cases. The kidneys were generally congested, and in some cases congestion appeared in the thymus and thyroids. The bladder was commonly contracted and empty. Petechiæ or hemorrhagic spots occurred on the heart in some cases but not often.

There was usually congestion of the surface blood vessels of the brain and sometimes clots between the cerebrum and cerebellum, or in connection with the medulla. The blood vessels of the meninges of the spinal cord were unusually full, and in some cases clots were found in the cervical or lumbar region, or in both. The liver, so far as appeared in the autopsies, was normal.

The outstanding conditions which may be considered as characteristic of poisoning by this plant are the abnormal quantity of gas in the alimentary canal and the lesions in the kidneys and the central nervous system.

PATHOLOGY.

Microscopic study of the various tissues from animals poisoned by *Asclepias galioides* confirms the autopsy findings and shows some changes not noted in the macroscopic examinations. The results of the studies made on tissues from 9 sheep, 1 steer, and 1 guinea pig show the lesions to be very uniform in character.

The most prominent conditions found are marked capillary congestion and a cloudy swelling of certain tissue elements which modifies the appearance of congestion. The organs most noticeably affected are kidney, lungs, heart, thyroid, thymus, and central nervous system, while minor changes are found in the liver, alimentary canal, and spleen. Thrombi occasionally occur in various organs.

KIDNEYS.

The lesions in the kidneys of the various animals differ some in detail, but in all there is pronounced albuminous degeneration of the epithelial cells lining the tubules, with marked swelling and disintegration of the cytoplasm. In places the swollen cells nearly fill the lumina of the tubules. Degenerative changes are most marked in the cells of the convoluted tubules, but may be largely due to their great bulk of cytoplasm. In certain instances the congestion is severe and general, but in most cases it is confined to relatively small areas. Greatly distended capillaries and veins occur, accompanied with considerable diapedesis and some edema. In such regions granules of blood pigment are abundant, showing that there has been a certain degree of destruction of red blood corpuscles. In some cases, many glomeruli are swollen, completely filling the capsule of Bowman, while others are edematous. Hemorrhages have occurred in a few glomeruli.

LUNGS.

Capillary congestion with diapedesis of erythrocytes and more or less severe transudation of serum into the alveoli is a quite characteristic condition in the lungs. In some cases there is a catarrhal condition of the bronchioles, with a marked exfoliation of the epithelium. In a few cases thrombi are found in some of the smaller veins.

HEART.

A study has been made of the wall of the left ventricle of the heart in the case of three sheep and one steer. The findings in these cases agree very closely. In the case of two sheep there is a very marked capillary congestion, with accompanying edema and some diapedesis of red corpuscles. In both these cases there is a mild degree of cloudy swelling, shown by the loss of cross striation and a somewhat granular cytoplasm. In the case of the steer and the other sheep the cloudy swelling has gone much farther. The muscle cells are markedly swollen and, except in certain restricted areas, the blood is squeezed out of the capillaries.

THYROID.

Samples of the thyroid gland were saved from 4 sheep, all of which showed pronounced capillary congestion.

THYMUS.

The thymus glands of 4 sheep and the steer were studied. All tissues of the glands of the sheep are very severely congested, the interlobular connective tissue and the medullary portion of the lobules being more hemorrhagic than congested. The blood in these areas obscures the tissues of the gland. The thymus tissues of the steer are not congested, but have been invaded by numerous eosinophile leucocytes.

NERVOUS SYSTEM.

The following portions of the central nervous system have been studied—cerebral cortex, cerebellum, hippocampus, medulla, and cervical and lumbar cords. In all parts there is a fullness of the capillaries which in some cases, especially in the spinal cord, is congestion rather than fullness. The varying condition found is simply one of degree. The most marked pathological condition found is in the cervical spinal cord of Sheep 492. In these sections there is pronounced capillary congestion, especially of the gray matter, with areas where hemorrhages have occurred. The perivascular and pericellular lymph spaces are much distended, as is the central canal. This condition exists in most of the sections of the central nervous system examined which included tissues from 4 sheep and 1 guinea pig.

LIVER.

The only change characteristic of Asclepias poisoning noted in the liver is a slight though well-marked cloudy swelling of the hepatic cells.

ALIMENTARY CANAL.

In the abomasum and intestines of the sheep and the steer the changes as a rule are not severe. They are largely vascular and in most cases vary from fullness to mild congestion. Here the effects of the high capillary pressure are well shown in the unusually full and prominent capillaries in the muscular layers. These vascular changes are perhaps most marked in the ileum, but while of the same general character, in some instances a well-marked congestion, with edema and diapedesis of red blood cells, also exists in the mucosa. In the mucosa of the ileum of the steer there is besides the unusual number of red blood cells a very pronounced invasion of eosinophile cells. In some cases there is a marked excess of polymorphonuclear leucocytes in the mucosa.

SPLEEN.

Changes in the spleen were not so pronounced as in the tissues previously mentioned. They consisted of a possible distention of a few cavernous veins and a few small areas of congestion and sometimes the presence of considerable blood pigment. Guinea pig 35 was of interest, as many of the endothelial cells show their phagocytic function containing one or more red blood corpuscles and indicating a certain degree of blood destruction.

TOXIC AND LETHAL DOSES.

Two head of cattle were treated experimentally. In determining the dosage the milkweed was in all cases estimated as green material. It was found, by experiment, that in drying, the plant lost, on the average, about 70 per cent of its weight, and the dosage was figured out on this basis. The dosage was also estimated as applying to a 100-pound animal. As 100 pounds may be considered the average weight of a sheep and 1,000 pounds the weight of a horse or steer, the dosage applies to the average sheep, or multiplied by 10 to the average horse or steer.

Of the cattle, No. 815 received a maximum of 0.294 pound without effect. No. 750 received 0.626 pound without showing any symptoms of intoxication. On the following day it was given 0.845 pound and became very sick; in this case, however, there is reason to think that the full quantity given was not eaten. About a month after this experiment it was given 0.551 pound with a fatal result. Just why 0.551 pound produced death and 0.626 showed no effect is not evident, for as shown elsewhere (p. 34) it does not seem probable that repeated feedings either increase susceptibility or produce toleration. However, from these experiments it seems probable that the toxic and lethal doses for cattle are not far from one-half pound per 100 pounds of animal.

Three experiments were performed with a horse. Horse 126 was made very sick by 0.22 pound per 100 pounds of animal, and later received 0.14 pound without effect. In 1919 it was killed by 0.193 pound. This last feeding, however, was of leaves only, and these have been shown to be more poisonous than the other parts of the plant. About 0.2 pound per 100 pounds, then, may be considered the probable toxic and lethal dose for a horse.

The following table shows the dosage of sheep from which positive results were obtained:

TABLE 2.—*Quantities of milkweed fed to sheep, with positive results.*

Sheep.	Quantity fed.	Result.	Sheep.	Quantity fed.	Result.
1918.			1918.		
No.	*Pound.*		*No.*	*Pound.*	
478	0.167	Sickness.	509	0.22	Death.
506	.148	Do.	437	.168	Do.
468	.167	Death.	1919.		
475	.161	Do.	372	.206	Sickness.
476	.27	Do.	534	.191	Do.
480	.577	Do.	542	.198	Do.
483	.138	Do.	522	.147	Do.
492	.165	Do.	522	.198	Do.
506	.184	Do.	461	.22	Death.

The number of experimental cases of sheep was sufficiently large to make the figures on dosage fairly complete. There were 10 cases of death and 7 of illness. Four animals were fed repeatedly, No. 509 three times, No. 506 five times, No. 478 six times, and No. 522 fourteen times, besides receiving feedings of marc three times.

It should be noted that Sheep No. 509 received the milkweed mixed with hay and ate it, so that the feeding was distributed over a number of hours—just how many was not determined. All the other sheep were fed by the balling gun, so that the material was received in a short time. There was, therefore, an opportunity for some elimination in the case of No. 509 and it may be expected that the effective dosage would be somewhat greater than in the other cases; this animal, after receiving smaller quantities in the preceding days, ate 0.22 pound per 100 pounds of animal between 11.10 a. m., June 22, and some time before 8.30 a. m. June 23.

Disregarding No. 509, however, and comparing only those sheep which were fed by the balling gun, the smallest quantity that caused symptoms was 0.148 pound with Sheep 506, and the largest quantity given without effect, except in those cases in which stems alone were fed, was to Sheep 522, 0.275 pound.

The smallest dose that produced death was 0.138 pound in the experiment with Sheep 483. It should be noticed that this lethal dose was somewhat smaller than the smallest toxic dose. An average of the fatal doses would not aid in determining the lethal dose, as an evident overdose was given in some cases, but 6 of the cases were killed by 0.184 pound or less.

From these cases it appears that the toxic dose is between 0.138 and 0.206 pound and that the lethal dose is from 0.138 to 0.22 pound. All these figures are computed on the basis of the green plant for a 100-pound animal.

It is evident that in *Asclepias galioides* we have an extremely toxic plant with very little difference between the toxic and lethal doses; No. 468 was killed by the same dose from which No. 478 recovered, and the smallest lethal dose is less than the smallest toxic dose in these experiments. The fact, too, that so many of the experimental cases died is evidence of the slight difference between the toxic and lethal dosage. The same thing is indicated in the high mortality of the range cases. The prognosis of poisoned cases is bad. In general, it may be stated that a dose of anything above 0.14 pound for a 100-pound sheep is liable to produce sickness or death.

Glover, Newsom, and Robbins give tentative figures for the dosage of 4 sheep, one of them dying on 63 grams, 0.139 pound, being practically the same as the minimum lethal dose of the authors of this paper. The weight of the sheep is not stated, however, and the plant was fed with consequent wastage and inaccuracy. In the Salina experiments all sheep were weighed and with one exception, Sheep 509, the plant was fed by the balling gun, so that the data were quite exact.

It must be remembered, too, that all these sheep were treated under corral conditions. It may be questioned whether the dosage would apply to sheep in pasture or on the range. Under the conditions which have existed in most recorded cases of poisoning, however, it is not probable that the dosage would have been much higher than in the experimental animals. In these reported cases, hungry animals have been more or less narrowly confined to areas on which the main vegetation was *Asclepias galioides*. Under such circumstances, as is well known, animals will eat large quantities in a very short time. Not only does their hunger make them eat rapidly and greedily, but jealousy of one another leads them to eat even more. It may be assumed then that grazing sheep may eat rapidly enough to make the dosage nearly or quite as small as in the case of the experimental animals. In comparing Sheep 509, which ate the plant, with grazing animals, it should be noted that range sheep do not eat so readily in corrals as on the range, and it is reasonable to suppose that a grazing sheep would be poisoned fully as quickly as a corral sheep.

SUSCEPTIBILITY OF DIFFERENT ANIMALS.

So far as the experiments show it appears that sheep and horses are about equally susceptible to poisoning from the plant. The method of feeding Sheep 509 and Horse 126 was the same, so that the two animals can be compared with each other. The lethal dose of the sheep was practically the same as the dose which produced violent illness in the horse. The dosage for Steer 750 was much greater, from which it seems probable that cattle are less susceptible than either sheep or horses. It does not follow, however, that horses are more liable to be poisoned than cattle, for horses are more particular about eating and there is less probability at any time of their eating any considerable quantity of injurious plants.

DELAY IN DEVELOPMENT OF SYMPTOMS.

The following table shows the time which elapsed after the plant was given before the symptoms appeared:

TABLE 3.—*Time elapsed between feeding of plant and development of symptoms.*

Animal.	Date and hour of feeding.	Date and hour of symptoms.	Time elapsed before symptoms.
1918.			*Hours.*
Horse 126	July 30, 3.35 p. m. to 5.15 p. m.	July 31, 7.45 a. m.	14
Steer 750	August 26, 12.05 p. m. to ——	August 27, 9.13 a. m.	21?
Steer 750	September 22,10.45 a. m. to 12 noon	September 23, 3.45 a. m.	15¾
Sheep 468	September 7, 11.12 a. m.	September 8, dead 7.30 a. m.	20
Sheep 475	August 17, 12.28 p. m.	August 18, died 6.30 a. m.	18
Sheep 476	June 20, 12.22 p. m.	June 20, 3.45 p. m.	3

TABLE 3.—*Time elapsed between feeding of plant and development of symptoms*—Continued.

Animal.	Date and hour of feeding.	Date and hour of symptoms.	Time elapsed before symptoms.
1918.			*Hours.*
Sheep 478	September 5, 2.30 p. m.	September 6, 11.35 a. m.	21
Sheep 480	June 18, 2.58 p. m.	June 18, 5.15 p. m.	2¼
Sheep 483	August 22, 11.10 a. m.	August 23, 7.15 a. m.	20
Sheep 492	September 11, 4.10 p. m.	September 12, 7.50 a. m.	15
Sheep 506	September 11, 4.15 p. m.	September 12, 9.30 a. m.	17
Sheep 506	September 20, 5.05 p. m.	September 21, 3.18 p. m.	22
Sheep 509	June 22, 11.10 a. m. to (?)	June 23, 8.30 a. m.	21?
Sheep 437	September 16, 4.25 p. m.	September 17, 7.40 a. m.	15
1919.			
Sheep 372	September 10, 6 p. m.	September 11, 8.55 a. m.	15
Sheep 461	September 6, 6.15 p. m.	September 7, 7.30 a. m.	13¼
Sheep 522	September 11, 6.55 p. m.	September 12, 8.40 a. m.	13¾
Sheep 522	September 22, 5.18 p. m.	September 23, 7.40 a. m.	14¼
Sheep 534	August 30, 6.30 p. m.	August 31, 7.40 a. m.	13¼
Sheep 542	September 3, 6.25 p. m.	September 4, 7.10 a. m.	12¾

It may be seen from the table that in 1918 it was about 14 hours after the horse had finished eating the plant before symptoms appeared.

In the feeding of the horse in 1919 it is not known when the feeding was completed, but apparently the symptoms of intoxication appeared in a shorter time.

Steer 750 was fed the first time about 12.05 p. m., and the first symptoms were noted about 9.13 a. m., the next day, a period of 21 hours. No note was made, however, of the time when the steer finished eating the plant, and it may be assumed that the period before evidence of intoxication was not more than 18 or 19 hours. At the second feeding there were symptoms in 15¾ hours after the feeding was finished.

In the case of sheep, information is lacking in regard to the incipience of symptoms in Nos. 468 and 475; it is not known when the feeding of No. 509 was completed. In regard to 14 sheep, however, notes were taken of the time when symptoms were first manifest. In these cases an average of the lapse of time between the feeding and the symptoms is 14.1 hours. The shortest time was 2¼ hours, in the case of No. 480, and the longest was 22 hours, in the case of No. 506. With the exception of Nos 476 and 480 all the cases lie between 15 and 22 hours.

One would naturally suppose that the larger doses would take effect in the shorter time, and an examination of the cases shows that this is true.

EFFECT OF REPEATED DOSES.

The repeated feedings which were given to several of the animals show significant results in regard to the questions of tolerance, increased susceptibility, and accumulation. Following is a tabulation of repeated feedings:

TABLE 4.—*List of repeated feedings and results.*

Animal.	Date of feeding.	Quantity fed per 100 pounds of animal.	Result.	Animal.	Date of feeding.	Quantity fed per 100 pounds of animal.	Result.
	1918.	*Pound.*			1918.	*Pound.*	
Steer 750....	Aug. 22	0.22	Not sick.	Sheep 470...	July 6	0.0473	Not sick.
	Aug. 25	.626	Do.	Sheep 470...	July 7	.0473	Do.
	Aug. 26	.845	Very sick.	Sheep 470...	July 8	.0473	Do.
	Sept. 22	.551	Death.	Sheep 470...	July 9	.05	Do.
Horse 126...	July 30	.22	Very sick.	Sheep 470...	July 10	.05	Do.
	Sept. 20	.140	Not sick.	Sheep 470...	July 11	.05	Do.
Sheep 478...	June 19	.165	Do.	Sheep 470...	July 12	.05	Do.
	Aug. 19	.110	Do.	Sheep 470...	July 13	.05	Do.
	Aug. 28	.138	Do.	Sheep 470...	July 14	.05	Do.
	Aug. 29	.138	Do.				
	Sept. 2	.147	Do.		1919.		
	Sept. 5	.167	Sick.	Sheep 522...	Aug. 11	.142	Do.
Sheep 506...	Aug. 26	.132	Not sick.	Sheep 522...	Aug 14	.155	Do.
	Sept. 11	.148	Symptoms.	Sheep 522...	Aug. 16	.162	Do.
	Sept. 12	.151	Not sick.	Sheep 522...	Aug. 18	.169	Do.
	Sept. 16	.160	Do.	Sheep 522...	Aug. 20	.176	Do.
	Sept. 18	.172	Do.	Sheep 522...	Aug. 23	.183	Do.
	Sept. 20	.184	Death.	Sheep 522...	Aug. 25	.191	Do.
Sheep 509...	June 20	.189	Not sick.	Sheep 522...	Aug. 27	.198	Do.
	June 21	.22(ate 0.2)	Do.	Sheep 522...	Aug. 29	.204	Do.
	June 22	.22(ate 0.24)	Death.	Sheep 522...	Sept. 1	.219	Do.
Sheep 470...	July 2	.0473	Not sick.	Sheep 522...	Sept. 6	.247	Do.
Sheep 470...	July 3	.0473	Do.	Sheep 522...	Sept. 9	.275	Do.
Sheep 470...	July 4	.0558	Do.	Sheep 522...	Sept. 11	.198	Symptoms.
Sheep 470...	July 5	.055	Do.	Sheep 522...	Sept. 22	.147	Sick.

Sheep 470, from July 2 to July 14, was fed a daily ration of from 0.05 to 0.0558 pound, receiving in the whole period a total of 0.6473 pound, with no resulting ill effects.

So far as cumulative effect is concerned, the 5 sheep and Steer 750 are the only animals that would have any bearing on the question. Sheep 470 received in 15 days about four times the toxic dose with no effect. Sheep 478, in addition to the feedings of June 19 and August 19, received on August 28 and 29 and September 2 doses equal to that which proved fatal for No. 483, yet on September 5 it was poisoned by an average dose, which was practically like that given on June 19 with no result.

In the case of Sheep 506, which on September 11 showed symptoms from 0.148 pound, slightly increased doses on September 12, 16, and 18 produced no results, and death was caused on September 20 by 0.184 pound.

Sheep 509, which was not affected by 0.2 pound on June 21, was killed the next day by 0.24 pound, which is probably close to the toxic or lethal dose for the plant as eaten by a sheep.

Sheep 522, besides having received three feedings of marc, was given 14 feedings between August 11 and September 22 of quantities varying from 0.142 pound to 0.275 pound. All the feedings except the last were of material from Palisades, Colo., which, as shown elsewhere (p. 37), was less toxic than that from other localities. On September 22 it was made sick by 0.147 pound of leaves from Rockville, Utah.

Steer 750, after a small feeding on August 22, received August 25 0.626 pound without effect, was poisoned on August 26 by an undetermined quantity, and killed September 22 by 0.551 pound.

In none of these cases is there any clear evidence that *Asclepias galioides* should be considered a cumulative poison. Neither did the fact that an animal had been poisoned once increase its susceptibility to the effect of the poison. It is doubtful, too, whether we are justified in thinking that any marked degree of tolerance is acquired by repeated feeding. Sheep 478 was not affected June 19 by 0.165 pound, but after repeated doses, ranging from 0.11 to 0.147 pound, was made sick on September 5 by 0.167 pound. Sheep 506 was given repeated doses with small increases until it was killed on September 20 by 0.184 pound, having shown symptoms on September 11 from 0.148 pound. This sheep, taken by itself, may possibly be considered as having acquired some tolerance, yet the difference between the fatal dose, 0.182 pound, and the toxic dose September 11 of 0.148 pound, is not great, and in the case of Sheep 478 the difference between 0.165 pound, which produced no results, and 0.167 pound, which produced symptoms, is negligible.

In the case of Steer 750 evidently no tolerance was acquired.

The experience with Sheep 522 may be considered as conclusive evidence that neither is the plant a cumulative poison, nor is any tolerance acquired by repeated feedings.

SEASONAL VARIATIONS IN TOXICITY.

The material from Hotchkiss, Colo., used in the experiments, consisted of young plants in bud. That obtained from Paonia, Colo., Rockville, Utah, and High Rolls, N. Mex., was in flower, while that obtained from Grand Junction, Colo., and Palisades, Colo., was in flower and fruit. The number of experiments was not sufficient to show definitely whether there is a variation in toxicity at different seasons or not, but so far as the work went the plant appears to be uniformly toxic at all ages.

No experiments were made with the plant cured and dried standing, but the numerous accounts of the loss of sheep when feeding upon the plant in this condition make it reasonably certain that it retains more or less of its toxicity. It follows that losses may occur at any time when the plant can be obtained and that hay containing any considerable quantity is dangerous.

RELATIVE TOXICITY OF LEAVES AND STEMS.

In the experiments of 1918 the whole plant was used. Inasmuch as it was desirable to know whether all parts of the plant were equally toxic, a number of experiments of feeding leaves only and stems only were made in 1919.

There were eleven feedings of stems of material collected at Palisades, Colo., the quantity fed varying from 0.147 pound to 0.404 pound. None of these feedings produced any effect, while one feeding of leaves, Sheep 461, 0.22 pound, caused death, and four feedings, Sheep 534, 0.191 pound, Sheep 542, 0.198 pound, Sheep 372, 0.206 pound, and Sheep 522, 0.198 pound produced toxic effect. Of the material collected at Rockville, Utah, three feedings of stems in quantities from 0.367 pound to 0.477 pound produced no effect, while Sheep 522 was made sick on 0.147 pound of leaves.

It is not to be inferred that the stems possess no toxic properties, but it seems very clear that the leaves are vastly more poisonous.

LOCAL VARIATIONS IN TOXICITY.

In the work of 1919, material was used from three localities, Paonia and Palisades, Colo., and Rockville, Utah. The Paonia material was used only in connection with the chemical work, either an extract or the marc being given. The Paonia collections had been used in 1918, however, showing that as small a quantity as 0.138 pound might produce death. The High Rolls material produced death on 0.16 pound. The relative toxicity of the Palisades and Rockville material was brought out quite clearly in the experiments of 1919. With the Palisades material death was produced in one case, Sheep 461 with 0.22 pound, while symptoms were caused by quantities varying from 0.191 pound to 0.206 pound. With the Rockville material Sheep 522 showed symptoms on 0.147 pound, while the horse was killed by 0.161 pound. That is, to produce intoxication, it took about a third more of the Palisades material than of that collected at Rockville. In this connection it should be noted that Sheep 548 received 0.176 pound of leaves from Palisades without effect.

While the Paonia, High Rolls, and Rockville materials were about equally toxic, the Palisades plants were much less so.

These differences in toxicity can not be explained by any seasonal change, and apparently are a local peculiarity.

REMEDIES.

Two animals, Sheep 437 and Sheep 506, were treated with atropin and morphin. The latter produced some effect in controlling the violence of the convulsions, but both sheep died and it did not appear that the remedy affected the final result.

On the theory that free action of the bowels might give relief, Horse 126 was treated with subcutaneous injections of arecolin and recovered. The same remedy was used with Sheep 478, Sheep 492, and Steer 750. Sheep 478 recovered, while Sheep 492 and Steer 750 died.

On the basis of the same theory. Sheep 372 and Sheep 461 were treated with eserin and pilocarpin. In both cases the eserin produced defecation. Sheep 372 recovered, while Sheep 461, which received a somewhat larger dosage, died. It is evident that the results from the use of arecolin and eserin were somewhat doubtful. While it seems probable that the course of the illness was somewhat modified, these drugs can hardly be considered as effective remedies.

From the character of the lesions in the central nervous system it seems probable that no remedy would be very effectual, and that little reliance should be placed on any kind of treatment. Possibly if a line of symptomatic treatment were followed with the same care with which a human patient is treated, the course of the illness might be modified, but such treatment is impracticable, and in any case a fatal result is to be expected in most animals.

ERADICATION OF THE WHORLED MILKWEED.

The apparent rapid increase of this weed in some sections, together with the fact that it is dangerous in hay as well as while green, makes the question of its eradication an exceedingly important one.

From what has been said of the habits of the plant, it is evident that its eradication will be a very difficult matter, for the young seedling, once started in a favorable location, begins to spread by adventitious buds from roots, being greatly aided by cultivation where cover crops are not grown. The rapid spread of the plant is aided by ordinary cultivation. The more the plant is broken, the better it thrives. Disk harrowing and plowing, without removal of the roots, simply helps to propagate the plant.

If the roots are exposed on the surface they will die, but every piece left in the ground becomes the possible origin of a new plant, and the greater the number of pieces, the larger will be the resulting crop. Plate IV, figure 2, shows a plant growing from a piece of root one-quarter of an inch long.

Presumably if tilled crops like beets, potatoes, and corn are grown, intensive cultivation by destroying the aerial parts of the plant will eventually have some effect, but it is a discouraging piece of work.

Cutting or mowing the milkweed before seeding, while it does not eliminate the plant, will accomplish much in preventing its distribution. This is especially important in driveways where hungry animals are trailed, and in locations like bedding grounds, where animals are herded close together. Had this been done in the "death patch" near Cortez, previously referred to, the losses would have been greatly reduced, if not entirely avoided.

Prevention of seeding of the whorled milkweed will stop the spread of the plant to a considerable extent. Mowing milkweed and destroying it, wherever it is common on range or trail, will solve the poison danger for the season, often saving thousands of dollars. Where the milkweed is growing in a meadow it should be carefully culled out by hand, for hay containing any considerable quantity of it is deadly to animals that eat it, and the hay therefore is worthless for feeding purposes.

PREVENTION BY CARE OF STOCK.

While it is not true that animals instinctively avoid injurious plants, it is true that they seldom eat them by choice. In the case of the whorled milkweed they seem to have an actual dislike of the plant, and eat it only when forced by hunger. This can be seen in many small pastures in western Colorado where whorled milkweed is abundant but forage is also plentiful, and the animals avoid the milkweed. Poisoning occurs when animals are confined in a pasture with little else to eat, when they are driven in a more or less hungry condition along trails where there is milkweed, or when they are on overgrazed ranges. It is evident that if the herder recognizes the dangerous character of the plant and uses suitable care, most losses will be avoided.

Care also should be taken, if hay from a milkweed region is used, to see that it contains no considerable quantity of the weed. If the weed is mature, as is generally the case, it is readily recognized by the pods.

SUMMARY.

The whorled milkweed growing in Colorado, Utah, New Mexico, and Arizona has been proved to be exceedingly poisonous.

The weed has been identified botanically as *Asclepias galioides.* In previous publications it has been cited as *Asclepias verticillata.*

The plant is poisonous to horses, cattle, and sheep, but most of the reported losses have been of sheep.

The most marked symptoms are the violent spasms. The autopsies and microscopical examinations show congestion of the peripheral blood vessels, the congestion being especially marked in some glands, the lungs, and the central nervous system.

The chemical examination of the plant, while incomplete, has demonstrated the existence of definite toxic compounds, part of which are glucosidal in nature. The plant contains also a minute quantity of nontoxic alkaloid.

There is no medicinal remedy which gives satisfactory results. Reliance must be placed on the destruction of the plant and such care of stock as will prevent hungry animals from coming into contact with masses of the weed.

LITERATURE CITED.

GLOVER, G. H.

1917. The Whorled Milkweed (*Asclepias verticillata*). Amer. Jour. Vet. Med., Vol. 12, No. 5, May, 1917, p. 303.

GLOVER, GEO. H., NEWSOM, I. E., and ROBBINS, W. W.

1918. A new poisonous plant. Agr. Ex. Sta. Colo. Agr. Col., Bull. 246.

GLOVER, GEO. H., and ROBBINS, W. W.

1915. Whorled Milkweed (*Asclepias verticillata*). *In* Colorado plants injurious to live stock. Agr. Ex. Sta. Colo. Agr. Col., Bull. 211, p. 60.

GRAY, ASA.

1886. Synoptical Flora of North America. Vol. 1, part 2, pp. 96–97.

HUMBOLDT, BONPLAND, and KUNTH.

1818. Nova Genera et Species Plantarum. Vol. 3, pp. 188–189.

VAIL, ANNA MURRAY.

1898. Notes on *Asclepias verticillata* and some nearly related species. Bulletin Torrey Botanical Club. Vol. 25, pp. 173–182.

1898. *In* Illustrated Flora of the United States, by Britton and Brown, Vol. 3, p. 12.

WOOTON and STANDLEY.

1915. Flora of New Mexico, pp. 510-511. (Contributions from the U. S. National Herbarium. Vol. 19.)

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