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MARSH, C. D. ; CLAWSON, A. B. 1 OF 1

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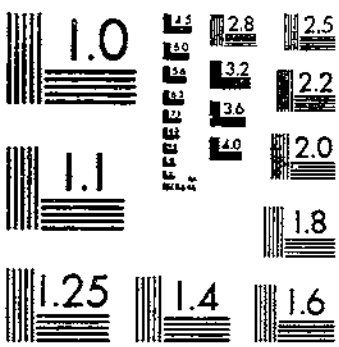

MICROCOPY RESOLUTION TEST CHART
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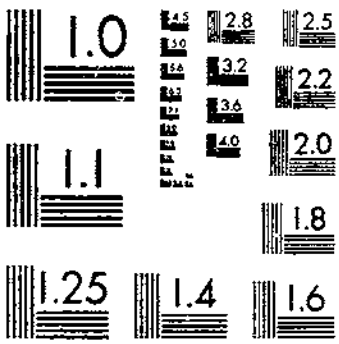

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NATIONAL BUREAU OF STANDARDS-1963-A

TECHNICAL BULLETIN No. 202 September, 1930

UNITED STATES DEPARTMENT OF AGRICULTURE
WASHINGTON, D. C.

TOXIC EFFECT OF ST. JOHNSWORT[1] (HYPERICUM PERFORATUM) ON CATTLE AND SHEEP

By C. DWIGHT MARSH, *Associate Physiologist in Charge of Investigations of Stock Poisoning by Plants*, and A. B. CLAWSON, *Associate Physiologist, Pathological Division, Bureau of Animal Industry*

CONTENTS

HISTORICAL REVIEW

The earliest published statement in regard to the poisonous properties of the species Hypericum was made by Cirillo (*4, p. 135*[2]) in his Fundamenta Botanicae, in 1787. It is presumed, although not positively known, that this is all that Cirillo published on the subject. A quotation from him was made in the Atti Del Real Instituto d'Incoraggiamento Alle Scienze Naturali di Napoli (*1*), of which the following is a translation:

(Hypericum crispum: A quick poison of white sheep; so that all which graze in the Tarentine fields are black; moreover, the wool among the rest is not so good as in the time of the Romans. Possibly this plant was then more rare. Cattle, on the other hand, feed upon *Hypericum crispum* with no harm; but if while they are eating this plant they, in licking with the tongue, moisten any part of their own body the skin is quickly deprived of hair. It is commonly, by the inhabitants, called Fumulo. It grows also in the fields of Sicily.)

The article mentioned also quotes from statements made by Signore Manni di Lecce, with some additional statements made by the author of the article, which was written without signature.

Signore Manni stated that the plant occurred toward the end of April and injured white sheep. The sheep, eating in the morning

[1] The name of this plant, as spelled here, is in accordance with the following publication adopted by the U. S. Department of Agriculture as authority for plant terminology: AMERICAN JOINT COMMITTEE ON HORTICULTURAL NOMENCLATURE. STANDARDIZED PLANT NAMES, prepared by F. L. Olmsted, F. V. Coville, and H. P. Kelsey. 546 pp. Salem, Mass., 1923.

[2] Italic numbers in parentheses refer to "Literature cited," p. 21.

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when the plants were covered with frost, get their chins and lips covered with moisture. Because of the unpleasant sensation, they rub the lips and chin on various parts of the body and thus distribute the poison. In a few days the wool falls off, the face swells, and there is general irritation over the whole body. They do not eat, and sometimes they lose their eyesight. Most of them die of convulsions within a short time; others may live for a few months, but finally die. The trouble is confined to white sheep, the black ones not being affected. The better-bred sheep are more likely to suffer from the poison. Sometimes the shepherds, when they find the sheep are poisoned, wash the faces of the animals in order that the poison may not be spread further. Signore Manni's statement that black sheep have more vigor than those with white wool and consequently are less likely to suffer is discussed in some detail. The article closes with a suggestion that it is desirable to perform some experimental work to determine whether the plant is harmful at all times of the day, and at all seasons; whether the flowers really contain the poisonous matter; whether the plant is poisonous in all countries; and to make a thorough study of the disease which produces a loss of wool.

The foregoing statements show that while Cirillo evidently thinks that sheep are poisoned by eating the plant, Manni apparently believes that the poison is carried to the various parts of the body in a mechanical way when the animals try to rub from their faces and lips the material that has become attached to them.

The first mention of the poisonous properties of *Hypericum perforatum* by an American author was the statement by Pursh in 1814 (*21*) that it "is considered very injurious to horses for, when they feed upon it, blindness and other diseases are said to be the consequence."

In 1843 Torrey (*27, p. 87*) wrote as follows:

> This pernicious weed is generally believed, in this country, to be the most common cause of "slabbers" in horses and horned cattle; and likewise to cause sores on their skin, especially in animals whose noses and feet are white, and whose skin is thin and tender * * *. Dr. J. M. Bigelow of Ohio states that he has known a high degree of inflammation of the mucous lining of the mouth and fauces produced by eating a few of the fresh leaves.

Darlington (*6, p. 58*) in 1826, remarked that the dew which collects on plants becomes acrid, and that he had seen the backs of white cows covered with sores, whenever the bushy ends of their tails had been applied after dragging through the St. Johnswort. In 1853 (*7, p. 28*), he stated that St. Johnswort—

> was formerly supposed to be the cause of scabs, and cutaneous ulcers among cattle especially white cows, and horses with white feet and noses. The fact was taken for granted, by the farmers: But it must be confessed, that although the plant continues to be abundant, the disease has nearly, if not entirely, disappeared.

In 1845 Morrell (*16, p. 374*) made the following statement:

> That pestiferous weed, called Johnswort, if growing abundantly where sheep are pastured, will cause an irritation of the skin, often over the whole body and legs of the sheep; but generally it is confined to the neighborhood of the mouth. If eaten in too large quantities, it produces violent inflammation of the bowels, and is frequently fatal to lambs, and sometimes to adults. Its effects when inflammation is produced internally are very singular. The writer has witnessed the most fantastic capers of sheep in this situation, and

once a lamb, while running, described a circle with all the precision of a circus horse: this was continued until it fell from exhaustion.

In 1849 Verheyen (*29*), in an article on the influence of certain agents on animals of different colors, the article being largely devoted to the effect of feeding upon buckwheat mentioned the data given by Cirillo, Marinosci, and Manni, in regard to *Hypericum crispum*. It is a matter of interest that Verheyen apparently was the first to connect the effect of these plants on the skin with the influence of the sun. Preceding authors had noted that only white animals, or those having white spots, were affected, but did not seem to have thought that this effect was produced locally on the body, because white animals, or white spots, were not protected from the sun's rays.

In 1852 Randall (*22, p. 271*) made the following statement:

Sore face.—Sheep feeding on pastures infested with Johnswort (*Hypericum perforatum*) not infrequently exhibit an irritation of the skin about the nose and face, which causes the hair to drop off from the parts. The irritation sometimes extends over the whole body, though no such case has fallen under my observation.

Paugoué (*19*), in 1861, gave in some detail the effect of *Hypericum perforatum* on horses which had eaten lucerne containing a large percentage of St. Johnswort. The symptoms which he noted were anorexia, depression, restlessness, dilated pupils, injected conjunctiva, and dermatitis. The animals were somewhat comatose, with a full, slow pulse, and a slow and deep respiration.

Randall (*23*), in 1863, in a somewhat extended discussion of the subject doubted whether the plant produced any injury to cattle or sheep.

In 1872 Rodet (*25*) gave a description of the plant and simply stated that it was reported to be injurious to sheep, and that experiments performed by him failed to produce any results.

Trabut (*28*), in 1898, said that in Tunis *Hypericum crispum* produced a disease of sheep known as hamra.

Chesnut (*3*), in 1898, said that the plant, Hypericum, was commonly believed to cause eruptions on cows' udders, and on the feet of white-haired animals. He quoted Doctor Bready, who had an experience with five poisoned horses in Maryland. The report made by Doctor Bready is in the files of the department and gives in considerable detail the symptoms of these animals. The main symptoms were sores, dermatitis, especially noticeable on white legs, resulting in ulcers and severe pain. There were sores on the lips and tongue. Doctor Bready took temperatures of the animals, and in all cases they were high, running up to 106° F. In these animals only the lips, tongues, and white areas were affected.

In 1904 Le Mouroux (*17*) published a general statement in regard to eczema on cattle with spotted skin, giving a description similar to those of his predecessors. He did not state that this eczema was caused by *Hypericum perforatum*, but it is to be presumed that this plant was the cause of the trouble.

In a paper published by Henry (*10*), in 1913, some details were given of the effect of St. Johnswort on horses which received the plant mixed with hay. Of the three animals fed on this hay, one black, and the other two with more or less white, the black was not affected

at all, but the other two were affected on the white parts of the body. The owner noticed that the dermatitis was more severe on the days during which there was a bright sun. Henry reported that it was not clearly stated whether the recovery of these animals followed their removal from the direct sunlight, but he assumed that the treatment given them was while they were in a stable.

He recorded the fact that the symptoms exhibited by these animals resembled very closely those produced by certain other plants under similar conditions. These plants included the clovers, especially *Trifolium hybridum*, and buckwheat. He stated that a fluorescent substance had been found in the buckwheat which became toxic when the animals were exposed to the sun through the absorption of the ultra-violet rays. It is very probable that the explanation in regard to buckwheat applies to St. Johnswort, inasmuch as the plant contains a similar fluorescent substance. In regard to treatment, he stated that as the trouble disappeared when the cause was removed locally, treatment was of little account. In the paper an abstract of preceding literature on the effects of this plant is given.

Rogers, in November, 1914, (*26*) published an article in which he gave the results of some experimental work with extract of *Hypericum perforatum* on guinea pigs and dogs. He found that 0.1 cubic centimeter of fluorescent extract given subcutaneously was a minimum lethal dose for guinea pigs weighing 250 grams each. In a dog the extract reduced the blood pressure and 0.5 cubic centimeter caused paralysis of the heart. He gave a somewhat extended account of the preceding literature and discussed in a general way the influence of light on white and pigmented skins in the Tropics.

In 1914 Ray (*24*) published a detailed account of the toxic effect of *Hypericum crispum*, which he said grew throughout northern Tunis, and was generally known by its Arab name of hamra. Its poisonous effects are well known there and much feared. He stated further that it affects sheep particularly, but is known to poison goats, cattle, and horses. The poisonous effects appear only in the light and only on animals which either are not colored or only partly colored. The symptoms are immobility, with the head falling low; then the unprotected areas of the skin become red and swollen, without any distinct rise of temperature. In sheep, goats, and cattle the ears, especially, are attacked; they, as well as the eyelids, become enormously swollen. In horses, itching on the injured areas results in biting and scratching until the skin is torn, and resulting scars may remain hairless. Sheep frequently lose their sight. Generally speaking, young animals are more susceptible than older ones, and improved breeds are more likely to be attacked than common animals. If white-skinned animals are protected from the light they are not affected by the plant. The Arabs stain the skin with solutions of tobacco or henna and thus protect the animals. In the plant is a fluorescent, red substance, which acts as a sensitizing agent to light. By the use of this fluorescent red pigment the author (Ray) was able to produce the disease.

Dodd (*8*), in April, 1920, besides giving a general summary in regard to *Hypericum perforatum* and its effects on cattle, sheep, and horses, reported experimental feedings of sheep with the plant. These animals showed the typical symptoms of Hypericum poisoning, the symptoms coming on at different periods, the minimum

period being 13 days. Apparently these were the first definite feeding experiments to prove the toxic properties of Hypericum.

Henry (*11*), in 1922, fed the plant to both cattle and sheep, using a younger stage of the plant than that employed by Dodd. On these animals typical symptoms of Hypericum poisoning were produced. Henry also performed a series of experiments to test the possibility of contact poisoning by the plant, the results of which indicated that such poisoning never occurs.

Lawrence (*14*), in 1922, stated that the plant was abundant in western Oregon and that cases of poisoning had been reported to the experiment station. He stated also that the plant is sometimes called goatweed and Tipton weed.

Lange (*13*), in 1922, gave a summary of the effect of the plant, stating that besides *Hypericum perforatum*, *H. maculatum*, and *H. pulchrum* were also poisonous.

Mélas-Joannidès (*15*), in 1928, stated that the effects of *H. crispum* are frequently noticed in goats and sheep in Greece.

In the foregoing review only those articles which deal specifically with Hypericum as a poisonous plant have been considered. There are a number of articles on the effect of light in producing dermatitis, and other symptoms of animals that have eaten certain plants; in these articles Hypericum is frequently mentioned, but its effects are not discussed in detail.

While, from the preceding historical review, it appears that *H. perforatum* has long been recognized as producing poisonous effects in a characteristic manner, there has been very little definite experimental work to determine the character of its effects or its dosage. Many inquiries had been addressed to the Department of Agriculture about the plant, to which the only information available for reply was that the plant was generally considered to be poisonous and that it was said to produce an inflammatory action on unpigmented surfaces of various animals. The supposed losses in the United States were not large, and, because of the large numbers of more important poisonous plants, no experimental work with *H. perforatum* was undertaken by the department before 1925. In that year A. W. Sampson, of the University of California, informed the department that the plant was making large inroads on the cattle and sheep ranges of northern California, especially in Humboldt County. It was thought that the plant popularly known as Klamath weed came into the region, through Del Norte County, from the Klamath River country, in Oregon. The plant was considered by the stockmen as a range pest, and an investigation was requested to determine ways of handling the situation. Doctor Sampson thought it especially important to determine definitely whether it was dangerous because of possible poisonous properties, and suggested a cooperative arrangement between the University of California and the Bureau of Animal Industry to begin feeding experiments. It was agreed that the university should arrange for the collection and shipment of experimental material, and that the bureau would carry on the experimental feedings at its station near Salina, Utah.

In accordance with this agreement, J. W. Logan, county agent of Humboldt County, made shipments of the weed to Salina, and the experimental feedings were carried on during the years 1925 to 1928, inclusive.

FIGURE 1.—St. Johnswort (*Hypericum perforatum*)

DESCRIPTION OF THE PLANT[3]

Hypericum perforatum Linn (fig. 1), common St. Johnswort, better known on the Pacific slope as Klamath weed, is also called goatweed, goatsbeard, Tipton weed, Eolaweed, amber, Penny John, rosin rose, herb John, Johnswort, and cammock. It is a perennial, smooth, erect herb, woody at base, growing from 1 to 2 feet high in eastern North America and in Europe; on the Pacific slope it often reaches 5 feet; stems simple, erect, 2-edged, branching freely by runners from the base which become erect, terminating in broad cymes. Leaves opposite, one-half to 1 inch long, numerous, sessile, oblong to linear, becoming revolute, obtuse, with pellucid dots. Cymes with numerous flowers, two-thirds to 1 inch broad; petals 5, yellow, edges black dotted; sepals 5, lanceolate, acute, much shorter than the petals; stamens numerous, clustered in from 3 to 5 groups; styles 3, capsules ovoid, one-fourth of an inch long, 3-celled; petals and stamens wither and remain on capsules; seeds numerous, cylindrical, and pitted. It increases rapidly both from seed and vegetatively by runners.

It is naturalized from Europe in temperate North America and introduced in Haiti and Chile. It was first introduced, in the grass and grain seeds of the early colonists of eastern North America, into the grasslands, pastures, and roadsides of New England, the Middle States, and eastern Canada. It now ranges from St. John's, Newfoundland, to western Ontario, southward to Virginia and the southern Appalachians, and westward to North Dakota, northeastern Iowa and Missouri.

It is unknown in the Rocky Mountain States and Provinces but is abundant in Oregon and California. Gilkey (*9*) states that it is found "throughout most of western Oregon, scattered colonies of little economic importance in eastern and central Oregon." Jepson (*12*) says that it is becoming a pest in abandoned or poorly tilled fields in the hill country in northern California (Tuolumne and Mendocino Counties to Siskiyou County) at altitudes from 500 to 2,300 feet.

In the east the first record is by Cutler (*5*), in 1785, for Essex County, Mass., as follows:

> Hypericum floribus *trigynis, caule ancipiti, foliis obtusis pellucido-punctatis*, Syst. Nat. St. John's Wort. Blossoms yellow. In fields, July–August. * * * The small dots upon the leaves, which appear like so many perforations, are said to contain an essential oil. The leaves are given to destroy worms. The flowers tinge spirits and oil of a fine purple colour.

Muhlenberg (*18*), in 1793, lists this plant from Lancaster, Pa. Barton in 1793 (*2*), lists *Hypericum perforatum* or common St. John's Wort as an introduced plant.

Probably the Oregon Trail pioneers of the forties and fifties carried the seeds from the Northeastern States to the Willamette Valley, Oreg. Piper (*20*), in 1906, gives Vancouver as the only locality he knew in the State of Washington where the plant occurred.

The first American manual to describe the species was that of Pursh (*21*), in 1814, as follows: *H. perforatum.* "In old fields,

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[3] The description of the plant was prepared by W. W. Eggleston, Bureau of Plant Industry. Acknowledgment is made to Mr. Eggleston also for calling attention to certain historical references.

meadows, and on dry hills; common. Common St. John's Wort has probably been introduced from Europe, but become one of the most pernicious weeds."

Although common in the East its control there has never been a serious problem. In the foothills of California conditions are quite different. The grasses and edible weeds of the pastures grow during the rains of the late fall and early winter. Cattle and sheep are pastured in the foothills at this time but large areas are reserved as "dry feed" for the next autumn before the rains start. Unfortunately the Hypericum thrives during the dry times of summer, growing taller and more thickly than in the East. Klamath weed fairly crowds out other plants in many areas of the foothills. Therefore, the need of methods of eradication is now a serious matter on the Pacific coast.

EXPERIMENTAL WORK

The experimental work included 31 feedings of cattle and 33 of sheep. Table 1 is a summarized statement of this work:

TABLE 1.—*Summary of feeding experiments with Hypericum perforatum*

Animal		Date of feeding	Method of feeding	Part of plant used	Plant given per 100 pounds of animal weight [1]		Place and date of plant collection	Result	Remarks
Designation	Weight				Total quantity	Average daily dosage			
CATTLE									
	Pounds				*Pounds*	*Pounds*			
No. 1043	689	Sept. 7–8, 1925	With hay	Stems, leaves, and fruit.	2.77	1.39	Eureka, Calif., August 1925.	Sick	Symptoms after 2.42 per cent in 1 day.
No. 1042	555	Sept. 14, 1925	do	do	5.04		do	Death	
No. 1102	562	June 14–15, 1926	do	Leaves, stems, and mature fruit.	1.00	.50	Eureka, Calif., September, 1925.	No effect	
No. 1101	608	June 17, 1926	do	do	1.50		do	Symptoms	
No. 1102	562	June 18–23, 1926	do	do	2.00	.33	do	No effect	
No. 1101	608	June 21–22, 1926	do	do	1.50	.75	do	Sick	
No. 1101	608	June 25, 1926	do	do	1.50		do	No effect	
No. 1105	496	July 26–27, 1926	do	Leaves and stems, second cutting.	1.18	.59	do	Symptoms	
No. 1069	509	July 28–Aug. 5, 1926	do	do	3.50	.39	do	Sick	Symptoms after 1.75 per cent in 2 days. Sick after 2.35 per cent in 3 days.
No. 1105	506	Aug. 13, 1926	Balling gun	Leaves, stems, and mature fruit.	1.25		Eureka, Calif., July, 1926.	Symptoms	
No. 1069	509	Aug. 16, 1926	do	do	1.50		do	No effect	
No. 1105	520	Sept. 3, 1926	do	do	2.00		do	Slight symptoms	
No. 1069	490	Sept. 6, 1926	do	do	2.53		do	Sick	
No. 1105	520	Sept. 10, 1926	do	do	3.00		do	Somewhat sick	
No. 1069	490	Sept. 13, 1926	do	do	4.00		do	Sick	
No. 1105	520	Sept. 20, 1926	do	do	4.50		do	Somewhat sick	
No. 1128	840	Aug. 21–Sept. 26, 1927	With hay	Leaves, stems, and fruit.	23.20	.75	Eureka, Calif., July and August, 1927.	No effect	
No. 1124	575	Sept. 6–21, 1927	do	do	24.00	1.50	do	do	
No. 1130	730	Sept. 6–22, 1927	do	do	21.24	1.25	do	Slight symptoms	Slight symptoms after 12.5 per cent in 10 days.
No. 1019	116	Sept. 6–22, 1927	Rubbed on face and ears.	do			Eureka, Calif., July, 1927.	No effect	
No. 1133	575	July 22–Aug. 30, 1928	With hay	Leaves, stems, and some flowers.	59.76	1.50	Fort Seward, Calif., July, 1928.	do	
No. 1133	665	Aug. 31–Sept. 15, 1928	do	do	43.44	2.71	do	Symptoms	Symptoms on Sept. 14, after 6.3 per cent in 1 day.

[1] Estimated as green plant.

TABLE 1.—*Summary of feeding experiments with Hypericum perforatum*—Continued

Animal		Date of feeding	Method of feeding	Part of plant used	Plant given per 100 pounds of animal weight		Place and date of plant collection	Result	Remarks
Designation	Weight				Total quantity	Average daily dosage			
CATTLE									
	Pounds				*Pounds*	*Pounds*			
No. 1134	535	July 30–Aug. 5, 1928	With hay	Leaves, stems, and some flowers.	5.00	.71	Fort Seward, Calif., July, 1928.	Symptoms	Symptoms after 3.5 per cent in 3 days.
No. 1134	610	Aug. 31–Sept. 2, 1928	do	do	5.00	1.67	do	No effect	
No. 1139	545	Aug. 1, 1928	do	do	3.50		do	Slight symptoms	
No. 1140	500	Aug. 10, 1928	do	do	4.00		do	Symptoms	
No. 1152	610	Aug. 13–16, 1928	do	do	4.05	1.01	do	Slight symptoms	Slight symptoms after 3.4 per cent in 2 days.
No. 1153	700	Aug. 19, 1928	do	do	5.13		do	Symptoms	
No. 1156	570	Aug. 27–30, 1928	do	do	5.00	1.25	do	No effect	
No. 1135	705	Sept. 4–7, 1928	do	do	7.24	1.81	do	do	Ate about 5 per cent on Sept. 4.
No. 1154	470	Sept. 5–9, 1928	do	do	6.00	1.2	do	Symptoms	Symptoms after 5.3 per cent in 1 day.
SHEEP									
No. 918	76.5	Sept. 10–18, 1925	do	Leaves, stems, and fruit.	10.46	1.16	Eureka, Calif., August, 1925.	No effect	
No. 917	79	Sept. 15, 1925	Balling gun	do	4.00		do	do	
No. 892	74.5	Sept. 21, 1925	do	do	6.00		do	do	
No. 945	143	June 14–July 14, 1926	With hay and bran.	do	44.96	1.45	Eureka, Calif., September, 1925.	do	
No. 940	106	July 28–Aug. 16, 1926	With hay and balling gun.	do	45.80	2.29	Eureka, Calif., July, 1926.	do	
No. 967	109.5	Aug. 31, 1926	Balling gun	do	6.00		do	do	
No. 978	114.5	Sept. 10–12, 1926	do	do	18.00	6.00	do	Somewhat sick	Symptoms after 12 per cent in 2 days.
No. 946	77.5	June 24, 1927	do	do	6.00		Eureka, Calif., August, 1925.	do	
No. 1000	54.5	June 27–28, 1927	do	do	4.20	2.10	Eureka, Calif., July, 1926.	Symptoms	Symptoms after 4 per cent in 1 day.
No. 1006	126	June 30–July 11, 1927	do	do	43.00	3.58	do	Sick	Symptoms after 8 per cent in 2 days.
No. 1015	95.5	July 21–Aug. 29, 1927	do	do	124.00	4.00	Eureka, Calif., July, 1926, and July, 1927.	Symptoms	Symptoms after 12 per cent in 3 days.
No. 1039	124	Aug. 23–24, 1927	do	do	5.33	2.67	Eureka, Calif., July, 1927.	No effect	Given 4 per cent the first day.

No. 1011	95.5	Aug. 25–Sept. 5, 1927	do	do	46.68	3.89	do	Symptoms	Symptoms after 12 per cent in 3 days.
No. 1029	114	Sept. 5–21, 1927	With hay	do	75.44	4.44	do	Slight symptoms	Slight symptoms after 70 per cent in 16 days.
No. 1030	78	Sept. 5–21, 1927	do	do	76.92	4.52	do	No effect	
No. 1040	44	Sept. 6–22, 1927	Rubbed on face and ears.	do			do	do	
No. 1033	106.5	Sept. 10–22, 1927	do	do			do	do	
No. 1053	76.5	Aug. 11–13, 1928	With hay	Leaves, stems, and some flowers.	10.44	3.48	Fort Seward, Calif., July, 1928.	do	
No. 1055	84	Aug. 11–13, 1928	do	do	9.52	3.17	do	do	
No. 1054	80	Aug. 12–15, 1928	do	do	16.24	4.06	do	Symptoms	Symptoms after 8.75 per cent in 2 days.
No. 1060	64.5	Aug. 13–15, 1928	do	do	4.64	1.55	do	No effect	
No. 1062	87	Aug. 14–15, 1928	From feed box	do	3.45	1.72	do	do	
No. 1063	105	Aug. 17–18, 1928	With hay	do	3.81	1.90	do	do	
No. 1066	124.5	Aug. 21–22, 1928	do	do	2.81	1.40	do	do	
No. 1067	120	Aug. 22–23, 1928	Balling gun	do	9.66	4.83	do	Symptoms	
No. 1070	115.5	Aug. 24, 1928	From feed box	do	3.46		do	No effect	
No. 1070	115.5	Aug. 30, 1928	Balling gun	do	7.00		do	Slight symptoms	
No. 1072	109.5	Aug. 28–Sept. 15, 1928	do	do	72.04	3.80	Eureka, Calif., August, 1927.	No effect	
No. 1058	92	June 11–July 31, 1928	From pan	do	204.00	4.00	do	do	
No. 1050	125	July 30–31, 1928	From feed box	do	6.40	3.20	Fort Seward, Calif., July, 1928.	Symptoms	Symptoms after 5.6 per cent in 1 day.
No. 1088	98	Aug. 1–3, 1928	With hay	do	2.04	.68	do	No effect	
No. 1058	104.5	Aug. 2–27, 1928	From pan	do	104.00	4.00	Eureka, Calif., 1927	do	
No. 1052	83	Aug. 3–5, 1928	With hay	do	4.80	1.60	Fort Seward, Calif., July, 1928.	do	

In one of the cases, cattle No. 1043, the plant was partly dried. In all the others air-dried plant was used. The figures for dosage are estimated on the basis of green plant, allowing 75 per cent for loss of moisture.

TYPICAL CASE OF CATTLE 1042

The history of cattle No. 1042 is especially interesting, because this is the only one that died as a result of eating *H. perforatum.*

Cattle No. 1042 was a yearling heifer, weighing 555 pounds at the time of the experiment. September 14, 1925, she was given three feedings of the plant at 10.55 a. m., 1.05 p. m., and 5.30 p. m. The dry plant was chopped and mixed with hay, and this material was kept before her from September 14 to September 17, but it is thought that none was eaten after September 14. It is evident that she had little appetite for anything after that day, and it is possible that the loss of appetite was an indication of the effect of the plant. All told, she ate about 7 pounds of plant, or a trifle over 5 per cent of her weight of plant, estimated as green. There was definite symptoms of effect during September 15. September 16 at about 8 a. m. her respiration was abnormal and the feces were soft. No other symptoms were noted during that day except a rapid respiration. On the morning of September 17 the respiration was irregular, and the animal was panting. This condition continued during the morning, the temperature, respiration, and pulse becoming more rapid, and the animal showing marked salivation. At 1.20 p. m. the temperature was 106.8° F., pulse 84, and respiration 160. Figure 2 taken at 12.50 p. m., shows the animal at the time when she was much salivated and her breathing was labored. During the afternoon she was up and down, being down most of the time with a continuation of the symptoms of the morning. As shown in Figure 3 the temperature continued high, reaching 108.5° F. in the evening, and the respiration and pulse rates were rapid. The respiration was at one time 160. Constant observations were made during the afternoon and up to 10.25 p. m. The animal became weaker as the afternoon went on. Figure 4, taken at 4.35 p. m., when the animal was on her feet, shows her attitude during this condition of weakness. The respiration continued not only fast, but irregular, and more or less labored. The feces were soft, and there was some drizzling of the

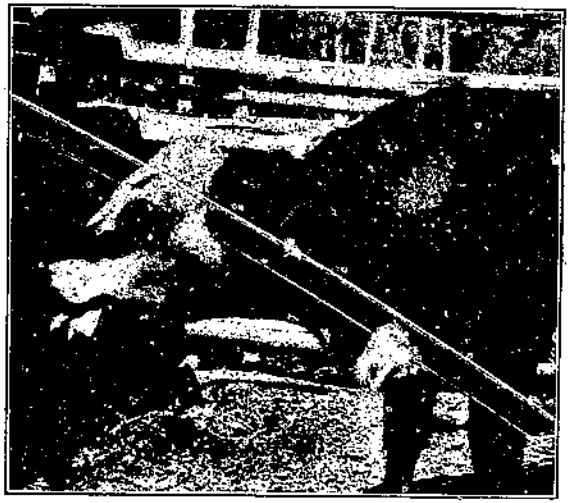

FIGURE 2.—Cattle 1042, showing salivation and labored breathing

urine. Decided weakness appeared the latter part of the afternoon, and when she endeavored to walk she dragged her hind feet and staggered. She was still able to get up, however, and continued rising at intervals until 10.25 p. m., the last observation of the day. September 18, at 6.40 a. m., she was found dead, lying on the left side. The body was still warm, so that death must have occurred in

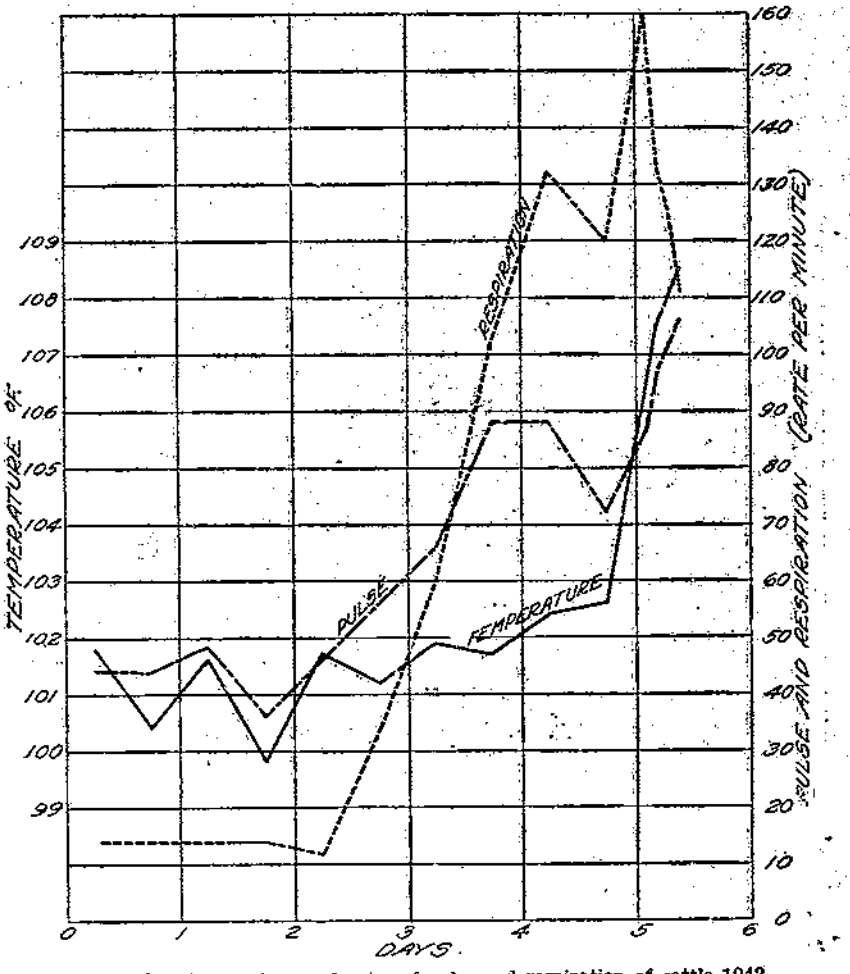

FIGURE 3.—Temperature and rates of pulse and respiration of cattle 1042

the latter part of the night. There was little evidence of struggling before death.

The autopsy was made at 7 a. m. Petechiæ and small hemorrhages were present on the ventricles of the heart, the pericardial fluid was somewhat excessive and bloody, and one part of the ileum was inflamed. The liver was very light colored, and the gall bladder much distended. The lungs were slightly congested and possibly edematous. The autopsy did not indicate any serious abnormalities.

The microscopical examination of the various organs added to the information obtained at the autopsy. The walls of the ventricles

were much congested in places, this being most marked near the endocardium of the left ventricle. Here there were severe hemorrhages which had extended a little distance into the myocardium and had surrounded some groups of muscle fibers, causing degenerative changes in them. In other portions of the myocardium the capillary congestion and edema were less severe. The liver parenchyma cells had undergone more or less degenerative change. In most cases this was little more than well-marked, cloudy swelling, but a few small necrotic areas were present, in which were many leucocytes. The spleen was somewhat congested and contained an abundance of hematogenous pigment. The kidney tubules were somewhat injured, the injury being of the acute, parenchymatous,

FIGURE 4.—Cattle 1042 in a very weak condition, the day before her death, which occurred four days after the experimental feeding

nephritic type. The changes here probably occurred shortly before the animal died. The lungs were somewhat congested, and a little serum and a few erythrocytes were found in the alveoli. The bronchial epithelium was somewhat swollen, and in some cases the bronchial walls were congested.

TYPICAL CASE OF SHEEP NO. 1015

Sheep No. 1015 was a 4-year-old ewe, weighing 95.5 pounds at the time of the experiment. She had been kept under observation from July 11, and experimental feeding was commenced on July 21. A feeding of 4 per cent of the animal's weight of *H. perforatum* was given daily from July 21 to August 20, by balling gun. The feeding was given in divided doses three times daily.

On July 23, the feces were abnormally soft, which was the first noticeable effect produced by the plant. On the next day, July 24,

the animal showed very distinct depression. From this time on, the animal showed increasing depression. The respiration was irregular most of the time, but it is doubtful whether the irregularity was caused by the plant, as a similar condition had been noticed before the plant was fed.

On August 1 there was evidence of irritation about the nose. From August 1 to 6 the temperature was somewhat high, and on August 2 the pulse rate was abnormally rapid. On August 2 she was rubbing her nose against the corral fence, presumably because of the irritation.

On August 3 a scabby condition was noticed on the nose between the nostrils. The nose was deep purple and somewhat swollen. This condition continued, although on August 7 the discoloration and swelling seemed to be somewhat lessened, and the next day the scabs were drying and peeling off.

On August 9, although the scabs had disappeared from the nostrils, there were patches on different parts of the nose and on the lower lip. On August 10 the areas of irritation were creeping up on the face, and there were minute scabs over the eyes and spots on the ears. These spots, with the exception of one on the right ear, had largely disappeared by August 14. On August 16 new scabs appeared below the eyes and above the right eye. These developed more strongly in the next day or two, but on August 20 this condition of irritation had very nearly cleared up and no more lesions appeared. The animal was in good general condition, and the signs of depression had largely disappeared.

On August 21 the sheep appeared practically normal and was turned into the pasture. Her weight at that time was 91 pounds. Considering her age, the animal maintained her weight fairly well during the experiment. It should be noted that while the depression and irritation about the face were without doubt produced by the plant, the irritation gradually disappeared while the plant was still being fed. The case was interesting as showing that while the plant presumably can produce a toxic effect, that effect is slight, and it is a matter of much doubt whether under range conditions any injurious effect would have been noticed. While the symptoms were not pronounced, the general character of the effect may be considered as typical of what may be expected from feeding *H. perforatum* to sheep.

DISCUSSION AND GENERAL CONCLUSIONS

SYMPTOMS

CATTLE

Twenty head of cattle were affected by the plant during the experiments. In 19 of these animals there was an increase in the rate of respiration. In some cases the respiration was irregular and accompanied by panting, but in only one of them could it be considered as distinctly labored. With this rapid respiration in 6 cases there was a higher temperature, and in 12 an abnormally rapid pulse. Soft feces were noted in 14 animals. In some cases this condition merged into a distinct diarrhea. Depression was noticed in 4. In addition to the symptoms which appeared in the other animals, cattle No. 1042, which died, had salivation, weakness, and a dribbling of urine. None of the animals, except the one that died, could be

considered as very sick, although the symptoms were distinctly marked in all. Because of the statements that feeding *H. perforatum* when the animals are kept in the sunlight is followed by a severe dermatitis on unpigmented areas, most of the experimental cattle were either white or had white spots, and were kept in bright sunlight. Few of them, however, showed any indication of such symptoms and none of them showed any serious dermatitis. The most marked case was cattle No. 1134, which was uneasy, continually switching its tail, and kicking with its hind feet. The brand scars were inflamed and covered with a serous exudate and were licked until they become raw. The behavior of the animal was apparently caused by a cutaneous irritation.

Cattle No. 1133 showed similar symptoms, switching its tail and licking the brand scab until the surface was raw and bloody; this animal, too, had areas of dermatitis on the muzzle. In cattle No. 1140 the brand scabs became inflamed and bloody, but there was no other evidence of irritation. Cattle No. 1130 had small scabs on the nose but no other symptoms. These four were the only cattle that showed any symptoms indicating skin irritation.

It is a matter of some interest that preceding authors do not mention the rapid respiration and pulse and high temperature which were noted in the cattle, nor do they cite cases of death without the production of the typical dermatitis.

SHEEP

In the feeding of sheep only white animals were used. Thirty-three sheep were fed, and of these 11 were affected. Seven had soft feces, and 3 had diarrhea. Four were distinctly depressed, and 6 were nauseated, 1 was vomiting. A higher temperature was noted in 8 and an increased pulse rate in 4. Respiration was accelerated in 1. One, No. 1006, was salivated. There was a dermatitis on the nose in 3 of the sheep, Nos. 1015, 1011, and 1029, and it appeared also in the ears; in 2 of them the dermatitis appeared also on the face. This was seen in small, scabby spots. In no case was it very pronounced. Sheep No. 1015, in which this condition was most noticeable, apparently felt the irritation, as it was found rubbing its face against the corral fence. In sheep No. 1011 the skin of the face seemed unusually sensitive.

The dermatitis seen in the sheep and cattle was very slight and not at all comparable with that which is said in literature to be characteristic of the effect produced by *H. perforatum* on white or white-spotted animals in the presence of sunlight. It may be significant that of the seven animals that exhibited dermatitis, cattle Nos. 1130, 1133, 1134, and 1140, and sheep Nos. 1015, 1011, and 1029, all but two were given the plant for five days or more.

So far as shown by these experimental feedings, it appears that cattle or sheep eating *H. perforatum* may have an increased pulse rate, a higher temperature, and rapid respiration. The abnormal characteristics of the pulse and respiration were more noticeable in the cattle than in the sheep. A laxative effect is produced on the bowels and this may become a diarrhea. A slight dermatitis may appear on the nose, face, and ears, and other parts of the body may be slightly hypersensitive. In no case, however, was there a severe dermatitis.

TOXIC AND LETHAL DOSAGE

SHEEP

The minimum toxic dose was in the case of sheep No. 1060, which received by balling gun 4 per cent of its weight in one day and showed slight symptoms. Sheep No. 946 was poisoned by 5 per cent received in one day and sheep No. 1050 on 5.6 per cent in one day. Sheep No. 1006 showed symptoms after receiving 8 per cent in two days. Sheep No. 1058 received 204 per cent of its weight in daily doses of 4 per cent with no effect, and sheep No. 1015 received 124 per cent in daily doses of 4 per cent, producing symptoms, but not of a serious character. It is evident that the experimental evidence in regard to the toxic dosage for sheep is very indefinite. It appears that a 4 per cent dose in one day may produce symptoms, but that some animals may receive this quantity daily for a long period without any effect. No sheep died.

CATTLE

The mimimum toxic dose in cattle was 1.18 per cent of animal weight given to cattle No. 1105 in two days with an average daily amount of 0.59 per cent.

The maximum ineffective dose was given to cattle No. 1133, 59.76 per cent in daily doses of 1.5 per cent. Cattle No. 1101 in two separate experiments was affected by 1.5 per cent given in one day.

Cattle No. 1042 was killed by 5.04 per cent eaten in one day. But cattle No. 1133 ate 5.9 per cent in one day and cattle No. 1135 ate 5 per cent without any effect. It appears that about 1 per cent may produce toxic effect and that about 5 per cent may be lethal.

However, as in the case of sheep, large quantities may be eaten, not only in single doses, but for a prolonged period without any harm.

While these results are far from giving definite data in regard to dosage, it is apparent that the plant is much more toxic for cattle than for sheep.

TIME FROM CONCLUSION OF FEEDING TO SYMPTOMS

With regard to the animals which received the plant in hay, there were no definite date as to the time at which the feeding was concluded, but this time was known definitely in the case of those fed by balling gun; the cattle fed by balling gun received the plant in a single feeding. Table 2 contains the data obtained from those cattle on the interval between feeding and the appearance of symptoms.

TABLE 2.—*Time elapsing between conclusion of feeding St. Johnswort and appearance of symptoms in cattle*

Cattle No.	Date of feeding	Time of first symptoms		Cattle No.	Date of feeding	Time of first symptoms	
		Hours	Minutes			Hours	Minutes
1105	Aug. 13	19	15	1105	Sept. 10	26	15
1105	Sept. 3	27	0	1069	Sept. 13	21	50
1069	Sept. 6	25	15	1105	Sept. 20	21	15

This table shows that the maximum time elapsing from the conclusion of the feeding to the onset of symptoms was 27 hours and the minimum was 19 hours and 18 minutes, the average being 23 hours and 29 minutes. It is rather surprising that the deviations from the average are no greater, especially as the dosage varied from 1.25 to 4.5 per cent of animal weight. There is no correlation between the length of time before symptoms appeared and the size of the dose.

Only two of the sheep received the plant in one day. Sheep No. 946 was fed by balling gun between 10.55 and 11.15 a. m., and again between 3.10 and 3.35 p. m. Symptoms appeared the next morning, 16 hours and 54 minutes after the conclusion of the second feeding.

Sheep No. 1070 was fed by balling gun five times between 10.22 a. m. and 4.54 p. m. The first symptom was noted 39 hours and 47 minutes after the conclusion of the last feeding.

Sheep No. 1067 was fed by balling gun two days. On the first day it was fed three times between 11.40 a. m. and 4 p. m., and on the following day it was fed twice between 11.08 a. m. and 1.30 p. m. Definite symptoms appeared 66 hours and 46 minutes after the conclusion of the last feeding.

All the other sheep were fed for several days and the symptoms appeared while the feeding was being carried on. In these cases of prolonged feeding the symptoms appeared at intervals varying from the second to the sixteenth day of the feeding.

While the experiments on both cattle and sheep were too few in number for any definite conclusions, there was considerable uniformity in the time required to poison cattle, whereas the time required to poison sheep varied widely. In general, the time before symptoms appeared was less in the case of the cattle.

DURATION OF SICKNESS

Table 3 shows the time elapsing from the first to the last-noted symptoms. The actual times during which the animals were sick were probably longer than those given in the table, as, when the animals were not under constant observation, they may have been affected before the first time noted, and there is also an indefiniteness about the conclusion of the sickness, inasmuch as the toxic effect may have continued somewhat after the last note was made. Cattle No. 1130 is not included in this table as it was returned to the owner before the dermatitis disappeared.

TABLE 3.—*Duration of sickness in cattle and sheep caused by feeding St. Johnswort*

Animal No.	Time sick			Animal No.	Time sick		
	Days	Hours	Minutes		Days	Hours	Minutes
Cattle:				Cattle—Continued.			
1043	2	4		1152	2		5
1042	[1] 1	22	8	1153	2	7	36
1101 (June 17)	1	8	35	1154	3	3	
1101 (June 21–22)	1	8	27	1133	3	16	
1105 (July 26–27)		18	5	Sheep:			
1069 (July 23–Aug. 5)	6	23		978	4	23	29
1105 (Aug. 13)	1	6	51	946		20	4
1105 (Sept. 3)[2]				1000		4	
1069 (Sept. 6)	1		30	1006	19		
1105 (Sept. 10)		23	40	1015	28		
1069 (Sept. 13)		21	50	1011	9		
1105 (Sept. 20)	2	6	5	1050	1	16	55
1134	4	20	5	1054	5		
1139		8	25	1067	4	8	27
1140	3		19	1070	2	23	55

[1] Sickness terminated in death.
[2] Sickness noted on 1 observation only.

Of the cattle that recovered, the maximum duration of the symptoms was in the case of No. 1069, which was sick for 6 days and 23 hours, following feedings between July 28 and August 5. The minimum time was in the case of cattle No. 1105, fed on September 3, on which only a single observation was made. The average of all the cattle that recovered, including No. 1105, in which a single observation was made, was 2 days, 3 hours, and 8 minutes. In the case of the animal that died, cattle No. 1042, the duration of illness was 1 day, 22 hours, and 8 minutes. A comparison of the duration of illness with the dosages shows that the larger doses were not correlated with the longer time.

The average duration of illness of the sheep affected by the plant was 7 days, 14 hours, and 29 minutes, the maximum being 28 days and the minimum 4 hours. A comparison of the period of sickness of the cattle and sheep shows that in these experiments the duration was distinctly longer in the sheep. The average duration in the sheep was approximately three times that in the cattle, and the maximum was about seven times.

However, in the cases of long illness of sheep the feeding was continued after the symptoms were noted. The feeding of cattle, on the other hand, ordinarily ceased with the appearance of symptoms.

The only published data in regard to the appearance and disappearance of symptoms are given by Dodd (*8*). About the only symptoms he noted were those connected with dermatitis. He says that a sheep was affected in 13 days of continuous feeding of the young plant before flowering on a variable daily dosage with a maximum of 4.5 pounds. The symptoms disappeared in about one month after the cessation of feeding; the feeding had been continued for 34 days from the beginning of the experiment.

EFFECT OF REPEATED FEEDINGS

Cattle No. 1011 was fed three times during the summer of 1926, cattle No. 1105 five times, cattle No. 1133 was fed continuously from July 22 to September 15, 1928, and cattle No. 1069 four times. It would seem possible from these repeated feedings to obtain information on cumulation or acquired toleration. Table 5 shows the results of these feedings.

TABLE 4.—*Results of repeated feedings of cattle*

Cattle No.	Date of feeding	Dosage, per cent of animal weight (green plant basis)	Result
1101	June 17	1.50 in 1 day	Symptoms.
	June 21–22	1.50 in 2 days	Sick.
	June 25	1.50 in 1 day	No effect.
1105	July 26–27	1.18 in 2 days	Symptoms.
	Aug. 13	1.25 in 1 day	Do.
	Sept. 3	2 in 1 day	Do.
	Sept. 10	3 in 1 day	Somewhat sick.
	Sept. 20	4.50 in 1 day	Do.
1069	July 28–Aug. 5	1.75 or less in 1 day	Sick.
	Aug. 16	1.50 or less in 1 day	No effect.
	Sept. 6	2.53 or less in 1 day	Sick.
	Sept. 13	4 or less in 1 day	Do.
1133	July 22–Sept. 15	1.3 to 6.3 daily	Symptoms Sept. 14, after 6.3 per cent Sept. 13.

In the case of cattle No. 1101, the same dosage, 1.5 per cent, was given three times, and in two cases was fed in a single day. In the first feeding, June 17, there was a slight effect. In the second feeding, June 21 and 22, given in two days, the animal was made sick. In the third feeding, three days later, given in one day, the animal was not affected. It might be inferred from the first two feedings that No. 1101 had an increased susceptibility because of the first feeding. The third feeding, however, would negative this inference. In this case there seems to be no evidence that either toleration or increased susceptibility was produced. In the cases of Nos. 1105 and 1069, no more definite conclusions can be drawn. The data simply seem to indicate that between a dosage of 1 or 1.5 and 4.5 per cent there is very little difference in effect, and taking the cases together it is not clear that there is either increased susceptibility or toleration. Cattle No. 1133 received 1.5 per cent of its weight daily from July 22 to August 30 with no effect; on August 31 it received 4.32 per cent with no result; September 1 and 2 it had a total of 2.59 per cent; on September 3 it had 5.9 per cent. The feeding was continued until on September 14 after eating 6.3 per cent on the preceding day, it showed symptoms. In the early feedings it received quantities that had been toxic in other cases. While there is a possibility that in this long-continued feeding it acquired a toleration for the poison, it is also possible that the animal may have had less susceptibility to the poison than others.

IMPORTANCE AS A STOCK-POISONING PLANT

While the experimental work showed that the *H. perforatum* from northern California may poison cattle and sheep, it is evidently not a very poisonous plant. Under range conditions there is doubt whether stock would eat enough to do any harm, unless feed were

so scanty as to produce nearly starvation conditions. This is very different from the statements quoted in the historical introduction in regard to Europe, northern Africa, and Australia, where the losses are said to have been serious.

Although many American authors have treated of the poisonous properties of this plant, they have drawn their material to a large extent, from European sources. While a number of cases of poisoning, supposed to be caused by St. Johnswort, have been reported in the neighborhood of Washington, D. C., one of which was reported by Chesnut (*3*) in 1898, there is little definite proof in North America to show the connection of this plant with any serious cases of poisoning. In 1863 Randall (*23*) expressed himself as very skeptical about the injurious character of the plant.

Without attempting to explain the serious effects reported from other parts of the world, the authors of this paper feel that there is every reason to think that this plant can not be regarded as an important poisonous plant in North America.

SUMMARY

St. Johnswort, *Hypericum perforatum*, has long been considered an important stock-poisoning plant in Europe, northern Africa, and Australia. Various observers have reported that domestic animals feeding on this plant developed inflammation and ulcers on unpigmented portions of the body, resulting in sickness and many times in death.

Cases of poisoning have been reported in the United States, but there has been no preceding experimental proof and the reported losses have not been large.

In recent years the plant has spread abundantly on the ranges in northern California and it seems desirable to settle the question of possible harmful effect of the plant when eaten.

Through a cooperative arrangement with the University of California, a quantity of the plant was collected at different times and fed to cattle and sheep during the years 1925 to 1928, inclusive.

Cattle and sheep were affected by these feedings, having high temperature, rapid pulse and respiration, tendency to diarrhea, and mild dermatitis.

Although the plant is evidently toxic, deaths rarely occur and ordinarily the poisonous effects are not very pronounced, and when so, only after a large dosage. Dermatitis was produced in only a few cases and in those was slight; the dermatitis was not at all comparable with that described in literature.

As one of the possible forage plants on the ranges of California St. Johnswort is not likely to be a source of much trouble because of its toxic properties.

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August 27, 1930

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