smelting centers, from Everett, Washington, about thirty miles north of Seattle, and from the region a few miles south of Salt Lake City, Utah, where several large smelters are in operation.[1] At both of these places complaints of injury to live stock have arisen from time to time. Only a few of these samples have been analyzed with the above results.

The writers wish to express their indebtedness to Dr. John Maxson Stillman for suggestions in regard to this work.

THE UNIVERSITY OF MONTANA, MISSOULA, MONTANA, AND STANFORD UNIVERSITY, CALIFORNIA,
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THE CHRONIC ARSENICAL POISONING OF HERBIVOROUS ANIMALS.[2]

(PAPERS ON SMELTER SMOKE, THIRD PAPER.)

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The two outbreaks of supposed arsenical poisoning which have led to the most investigation from a scientific standpoint, are the one in Manchester, England, in the year 1900, and that in the district surrounding Anaconda, Montana, during the year 1902-1903. The former was confined to human beings, the latter almost entirely to cows, horses, and sheep. As yet very few data have been obtained to show whether or not the effects of the arsenic in the latter case extended to the human beings who resided in the district.

During the latter part of November, 1902, it was the fortune of one of us to travel over about one hundred square miles of the territory surrounding the new Washoe smelter at Anaconda. At that time the carcasses of several hundred animals that had recently died lay scattered over various ranches of the valley, and one ranch was visited where approximately sixty carcasses, mostly horses, were seen in a group in one corner of the field. A very large number of the animals were dissected, and practically all of them gave evidence of arsenical poisoning, either acute or chronic.

As has been explained more in detail in a former paper, what was called the "Old Works" had been in operation for many years on the north side of the valley of Warm Springs Creek, in which the city of Anaconda is located. In January, 1902, smelting operations were transferred to the "New Works," which are located on the south side of the same valley, on a ridge extending down from the foot-hills. This ridge projects into the Deer

[1] See Ebaugh, Gases *vs.* Solids, THIS JOURNAL, **29**, 951, 970 (1907).

[2] At the New York meeting of the American Chemical Society, December, 1906, W. D. Harkins presented a similar paper including only his own work. The first paper of this series deals with the amount and character of the smoke given off by the smelter, and the second treats of the arsenic content of the vegetation.

Lodge Valley in such a way that much more of the smoke from the smelter was blown across or into the valley than during former years.

Although the smelter was in operation during the whole year, few cases of serious sickness among live stock were noticed until September, from which time the number of deaths increased rapidly until November, when a maximum was reached. This is easily understood when the facts of the case are considered as presented in the second paper of this series.[1] The fresh grass of the spring has little time to accummulate arsenic from the air, and the summer is a period of rapid growth and frequent rains; in the autumn comes a dry period during which there is no plant growth, so this is the most favorable period for a rapid increase in the amount of solid substances adhering to the leaves and stems of the plant. During this dry period, the farmers were forced to drive or ship a great number of animals from the district, and those remaining were stabled and fed upon hay. The owners had found from their experience with the symptoms exhibited by the animals, that the disease was greatly moderated by changing the diet from grass to hay. This was explained by the much smaller amounts of arsenic found in the latter.[2]

In 1903 the smelter company had built the great flue and stack described in the first paper[3] in order to prevent the escape of the arsenic. In accordance with an agreement entered into with the farmers, the smelter was shut down from July 1st to September 30th of this year, and when the plant was started on the latter date the smoke was supposed to no longer scatter poisonous substances over the valley, since it was passed through the flue intended for its purification. During the summer and autumn of this year there were very few cases of death among the animals of the valley and it was believed by the residents of the valley that there would be no more cases of sickness due to arsenic.

Two interesting exceptions were investigated in cases where the farmers thought that arsenical poisoning had occurred. A drayman in the city of Anaconda purchased a load of hay, supposed by him to have been grown during the year 1903. After feeding the hay to his horses for about a week one of them sickened and died, the most marked symptons before death being recurrent convulsions. A post-mortem examination showed the usual inflamed condition of the stomach, and the presence of a number of small ulcers, resembling those frequently observed in cases of arsenical poisoning. An analysis of the hay gave 0.0285 per cent. (285 parts per million) of arsenic trioxide. Various tissues of the animal were also analyzed and the liver found to contain 1.30 milligrams of arsenic trioxide to one hundred grams of tissue (13 parts per million). It seemed improb-

[1] THIS JOURNAL, preceding paper.

[2] Table 3; or Table I, preceding paper.

[3] THIS JOURNAL, 29, 971–3 (1907).

able that hay which contained so much arsenic could have been grown in the year when the smelter was closed for the three summer months, and upon investigation it was found that the hay had been grown about three miles north of the smelter during the preceding year.

In October, a sheep owner who lived about twenty-eight miles from the smelter, and in a small valley somewhat protected from the smoke by an intervening range of hills, found that his grass was becoming exhausted. He rented a low field lying approximately fifteen miles northeast of the smelter, and drove his three thousand five hundred sheep from his home to this field, upon which there was a large amount of grass. After pasturing there for a week, a number of the sheep became sick, and the neighbors advised the owner to drive the flock to a feeding place farther from the smelter. On the way home five hundred sheep died, but during the next four weeks the mortality diminished. The total loss was six hundred and twenty-five animals. The case was investigated by the state veterinarian, Dr. M. E. Knowles, who decided that the sheep had died from acute arsenical poisoning. The four samples submitted by him for analysis gave the following results:

TABLE 1.

Number.	Organ.	Parts As_2O_3 per million.
1	Stomach	3.1
2	Stomach	Trace
3	Stomach and liver	3.0
4	Stomach and liver	4.0

Claims were made that the sheep had died from poisoning caused by the alkali of the soil. A complete analysis of the soil, and a partial analysis of the stomachs of the sheep, showed that this was not true. It is a fact that the soil was high in the salts of the alkalis, containing 0.70 per cent. soda (Na_2O), 1.38 per cent. potash (K_2O), 0.40 per cent. sulphuric acid (SO_3), 0.00306 per cent. arsenic trioxide, 0.0118 per cent. copper, together with lead, a trace of antimony, etc.

A visit was made to the field to see if the cause of the death of the sheep could be determined. The grass was cropped very close to the ground, and over the lower part of the field there was a large amount of moss which had been greatly disturbed, presumably by the sheep during their feeding. On analysis it was found that the grass contained fifty-two, and the moss four hundred and five parts of arsenic trioxide in a million. It was therefore a reasonable assumption that the sheep had been poisoned at first by eating the grass, and in a greater degree by eating the moss at a time when the grass was nearly exhausted. It is probable that the sheep were very hungry when they first reached the field as they had lived for some time upon a meagre food supply.

There were no more complaints of serious damage from the farmers, so far as the effects of arsenic were concerned, until late in the autumn of 1904. It is true, that, while the effects of sulphur dioxide upon the plants had been moderated on the average, it had become more severe at many points some distance from the smelter. The charge began to be made by the farmers that the same was true of arsenic, and that symptons of arsenical poisoning had again manifested themselves in spite of the use of the big flue and stack. Chemical investigations were actively renewed in January, 1905, and have continued up to the present time. The results of the analyses of smoke and forage have been given in the previous papers of this series. A reference to these will show that enormous quantities of arsenic were thrown out by the high stack, and that large quantities were present on the vegetation.

Autopsies of a large number of animals were made, and many of the samples analyzed. Great care was taken with all of the analyses so that quantitative results of considerable accuracy might be obtained, and some of the precautions used will be described in a subsequent paper. The methods were first tested by analyses upon known amounts of arsenic. Various substances were used in the decomposition of the tissue, but the methods of Fresenius, von Babo, and Chittenden-Donaldson were adopted almost exclusively. All reagents were scrupulously purified from the most minute traces of arsenic, and were tested very frequently during the course of the analyses. All of the glassware, glass tubes, rubber tubes, porcelain-ware, etc., were tested to see if they would give traces of arsenic when used in the manner necessary for the tests. Berlin porcelain was used to the exclusion of glassware, except for the Marsh apparatus, which was made of Jena glass.

A modified Chittenden method which was much used in cases where little fat was present, consisted in putting 100 grams of the sample into a large casserole, and adding 100 cc. of nitric acid. The mixture was stirred frequently until it had become liquid, and was then heated on an asbestos board which rested on an electric stove. After heating for a half hour longer the solution was cooled, and thirty cubic centimeters of concentrated sulphuric acid added. The solution was heated until it began to turn brown, and then the steam of a dropping funnel was introduced through a hole in the watch glass cover, and nitric acid allowed to drop into the hot solution just rapidly enough to keep it from turning dark. After this addition has been kept up for some time, the solution could be evaporated (while adding nitric acid drop by drop) until the fumes of sulphuric acid appeared, without a blackening of the solution. A part of the sulphuric acid was then evaporated, nitric acid being occasionally added. The cooled solution was diluted and re-evaporated in order to remove oxides of nitrogen which might be present, and the cooled and diluted solution used for the determination of the arsenic by a modified Marsh method. The generator was kept active for six hours, stannous chloride being used to increase the activity of the zinc. It was found that this length of time was essential where weighable quantities of arsenic were determined. The best results were obtained by the use of a special fire-brick furnace with four very large burners. A second hard glass tube lying in a second furnace was connected with the first in order to test the completeness of the decomposition of the arsine, and arsenic was always found in this tube in cases where action in the generator became at all rapid.

The results of the analyses of a part of the animal samples are given in Table 2.

TABLE 2.—AMOUNTS OF ARSENIC IN THE TISSUES OF ANIMALS.

No. and organ.	Date.	Animal.	Distance.		Parts As_2O_3 per million.
	1902				
1 L	Sept.	Horse	3	NW	4.7
2 L	Sept.	Horse	2	SSE	1.1
3 L	Sept.	Horse	5	SE	2.8
4 L	Sept.	Horse	5	SE	0.8
5 L	Sept.	Cow	3	E	11.3
6 L	Sept.	Calf	3	S	6.2
7 L	Sept.	Calf	1.5	S	0.4
8 L	Sept.	Calf	1.5	S	0.3
9 L	Sept.	Steer	3	NE	8.6
	1903				
10 S	Oct.	Sheep	15	NNE	3.1
11 S	Oct.	Sheep	15	NNE	Trace
12 L & S	Oct.	Sheep	15	NNE	0.7
13 L & S	Oct.	Sheep	15	NNE	4.0
14 L	Oct.	Horse	1.5	NE	13.0
	1905				
15 L	Jan.	Filly	3	N	0.01
16 Lu	Jan.	Geld	5	E	7.1
17 S	Jan.	Geld	2	SW	0.01
18 L	Jan.	Cow	6	SE	3.3
19 L	Jan.	Geld	4.5	NNE	35.0
20 K	Jan.	Mare	14	NNE	13.3
[1]21 L	Jan.	Colt	2	S	2.6
22 L	Jan.	Cow	3	SW	1.6
[1]23 L	Jan.	Cow	3	SE	2.1
24 L	Jan.	Cow	5	NE	11.9
25 L	Jan.	Cow	5	NE	10.3
26 L	May	Steer	13	NNE	0.01
27 L	May	Cow	6	N	0.01
28 L	Nov.	Cow	13	NNE	10.00
29 L	July	Cow	2	S	7.4
[1]30 L	Jan.	Sheep	8	N	0.01

[1] The shoulder of colt 21 was covered with a green fat which contained 288 parts of copper to the million. Sample 30 L contained 592 parts; and sample 23 L, 88 parts of copper to the million.

TABLE 2 (*Continued*).

No. and organ.	Date.	Animal.	Distance.	Parts As_2O_3 per million.
31 L	Jan.	Sheep	3 N	6.8
32 L	Jan.	Calf	2 S	1.5
33 L	Jan.	Calf	3 SW	6.5
34 L	Feb.	Calf	2 S	1.3
	1906			
35 L	Nov.	Geld	3 S	6.0
36 L	Oct.	Geld	4 N	3.4
37 L	Aug.	Mare	4.5 NE	4.4
38 L	Aug.	Geld	1.7 SSW	3.9
39 L	Aug.	Horse	5 NNE	16.1
40 L	Aug.	Horse	5 NNE	9.5
41 L	Jan.	Mare	5 NNE	1.3
42 L	Sept.	Geld	4.2 NNE	14.8
43 K	Jan.	Mare	15 N	2.1
44 L	Jan.	Mare	15 N	8.7
45 L	Jan.	Geld	10 NNE	7.6
46 L	Jan.	Geld	3 N	5.3
47 L	Feb.	Filly	4.5 NNE	3.1
48 L	Feb.	Filly	5 N	17.8
49 L	Feb.	Mare	4.5 NNE	8.7
50 Br	Feb.	Mare	4.5 NNE	4.5
51 H	June	Filly	4.2 NNE	460.0
52 L	Mar.	Horse	1.5 S	20.7
53 L	Aug.	Mare	12 NNE	4.99
54 B	Aug.	Mare	12 NNE	20.67
55 L	Sept.	Horse	4.5 NNE	Trace
56 L	Sept.	Mare	6.5 SE	52.5
57 L	Sept.	Geld	4.5 NNE	3.3
[1]58 K	Feb.	Colt	4.5 NNE	19.8
59 L	Feb.	Colt	10 NNE	Trace
60 L	Feb.	Colt	4.5 NNE	25.5
61 L	July	Colt	3 NNE	31.7
62 L	July	Colt	2 S	4.4
63 L	Nov.	Colt	9 NNE	2.6
64 L	Oct.	Colt	2 S	4.7
65 L	Aug.	Colt	8 NE	2.2
66 L	July	Colt	8 NNE	1.1
67 L	Feb.	Cow	10 N	11.8
68 L	Feb.	Cow	3 SSE	33.8
69 L	Nov.	Cow	13 NNE	10.0
70 L	July	Cow	3 N	14.2
71 K	July	Cow	3 N	6.2
72 L	July	Cow	3 N	63.12
73 L	Nov.	Cow	3 SSE	9.2
74 U	Nov.	Cow	3 SSE	16.0
75 L	Nov.	Cow	10 NNE	1.2
76 L	Nov.	Cow	4.2 NNE	10.4
77 L	Jan.	Steer	5 E	5.4
78 L	Oct	Calf	1.7 SW	16.2

TABLE 2 (*Continued*).

No. and organ.	Date.	Animal.	Distance.	Parts As_2O_3 per million.
79 L	Feb.	Calf	3 SSW	6.3
80 L	Jan.	Sheep	10 N	8.9
81 L	Aug.	Sheep	4.2 NNE	5.0
82 L	Sept.	Pig	1.7 SSW	Trace

L represents a sample of the liver; B, of the bone; Lu, of the lungs; U, of urine; H, of hair; K, of kidney; Br, of brain; S, of stomach. The animals represented by samples 1 to 42 were more emaciated on the average than those represented by samples 43 to 82.

The number of parts per million multiplied by seven-tenths gives the number of grains of arsenic trioxide to one hundred pounds of tissue. In this way a comparison may easily be made with the recommendation of the Royal Commission on Arsenical Poisoning:[1]

"In our view it would be entirely proper that penalties should be imposed under the sale of Food and Drugs Acts upon any vender of beer or any other liquid food or of any liquid entering into the composition of food, if that liquid is shown by an adequate test to contain 1/100 of a grain or more of arsenic in the gallon; and with regard to solid food—no matter whether it is habitually consumed in large or small quantities, or whether it is taken by itself (like golden syrup) or mixed with water or other substances (like chicory or 'carnos')—if the substance is shown by an adequate test to contain 1/100th grain of arsenic or more in the pound."

According to this recommendation a large number of the samples of liver given in Table 2 would be considered as deleterious when taken as food by human beings, and in one case a cow's liver contained forty-three times the maximum amount allowed in food by the commission. Flesh and also milk were found which exceeded the limit prescribed by the commission.

The livers of animals, according to Table 2, contained from a trace to 63.12 parts of arsenic trioxide to one million parts of tissue. The maximum number was obtained in a case of acute poisoning which occurred about three miles north of the smelter. This seems a strange case when it is considered that, although the grass of the ranch has usually contained a large amount of arsenic, at the time the cow died the percentage was relatively low, being between thirty and forty parts to the million.

An effort has been made to trace a relation between the quantity of arsenic ingested with the food, and that contained in the livers of the animals, but this has been impossible. It is true that the amounts of arsenic are larger on the average in cases where the animals were kept close to the smelter, but it is obvious that the condition of the animal is the more important factor in determining the amount of arsenic retained by the tissues.

[1] Final Report Royal Commission on Arsenical Poisoning, p. 50 (1903).

The amounts of arsenic present in the organs of the animals is in many cases small, yet no smaller than might reasonably be expected in chronic arsenical poisoning following the repeated and regular administration of moderate doses of arsenic. Before the time of this investigation, very little experimental work had been done on horses and cattle in which accurate analyses had been made of the organs following arsenical poisoning. In a case reported by the Russian Minister of the Interior, the liver of a cow which had been fed considerable amounts of arsenic for a period of six months, contained 0.13 part of arsenic per million. Spallanzani and Zappa[1] fed a cow from 0.4 to 0.5 gram (6 to 8 grains) of arsenic trioxide daily for 44 days and the following results in parts of arsenic per million were obtained from an analysis of the viscera:—stomach, 19; liver, 11; kidneys, 4.5; spleen, 7.6; lungs, 3; muscles, 3.8.

In order to see how the results of Table 2 would compare with those obtained from animals killed by arsenic, and also in order to secure data as to the poisonous dose, horses were fed upon arsenic in different forms. The doses given were large as the time for the experiments was very short. A horse was fed upon flue dust containing a total of 20.65 per cent. of arsenic calculated as trioxide, and 17.89 per cent. of soluble arsenic, also calculated as trioxide. Considering only the soluble arsenic, the horse was fed two grams of arsenic trioxide for eighteen days in addition to hay containing about 0.0030 per cent. In the liver was found 3.5 parts, and in the kidneys 18.0 parts per million, an amount for the liver which was less than the average of the values given in Table 2. A second horse was given 2.8 grams (0.1 oz.) of arsenic trioxide in two doses, on the first day mixed with bran, and on the second ingested as a drench. On the fourth day the animal died, and on analysis the liver was found to hold 8.7 parts per million. A third horse died on the third day after having been given two doses of 7.5 grams each, one on the first, and one on the second day. The liver contained 12.2 parts, while that of a sheep which had been fed arsenic for some weeks contained 11.9 parts to the million.

In taking samples during the first few years of the case, the more emaciated animals were usually selected, but beginning with January, 1906, a larger number of those that were fat and in a seemingly good condition were chosen. The result of this change of policy is shown in the table, where the average content of arsenic for 1906 is much higher than for previous years.

The elimination of arsenic probably begins very early and persists during the whole period of its absorption. In the human subject it often appears in the urine within five hours after ingestion, and may continue to be eliminated for thirty days after the last dose is taken. This is unusual, however, fifteen days usually sufficing to remove almost all of the arsenic

[1] *Annal di Agricoltura*, 131, 25.

from the human system. The difficulty in finding in the tissues any considerable amount of arsenic—an amount for example, sufficient to prove on the basis of a chemical analysis alone that death was due to arsenical poisoning, lies here. And where the case is one of chronic poisoning extending over a long period, and caused by a fairly constant amount of the poison being ingested daily, the isolation of an amount approximating a toxic dose is often impossible, simply because a really toxic dose was never taken at one time, and what was taken was partly excreted by the kidneys even before its absorption from the stomach and intestines was complete.

The proof of poisoning is complete, (1) "when the symptons known to be caused by the poison have been observed during life; (2) when the post-mortem examination shows the presence of such lesions as it is capable of producing, and the absence of other causes of death; (3) when the toxic agent is demonstrated to be present in the cadaver or dejecta of the animal poisoned." It is not always possible to present evidence along all these lines, for it has often occurred, even with a poison so prompt in its action and of such certainty of detection as arsenic, that life may be prolonged for a sufficient length of time to permit the total elimination of the poison, and death results from its action by a continuation of the morbid processes which it established. Again one of the symptoms of chronic poisoning through arsenic is loss of appetite, so that often during the last few weeks or days of life, little or no food is taken. Then where the poison accompanies the food, and is proportionate to it in amount as in the cases at issue in this investigation, failure to take any considerable amount of food during the last few weeks of life, stops the ingestion of the poison and allows the system to expel all or nearly all the substance before death ensues. In certain of the cases given in Table 2, animals apparently in a diseased condition were slaughtered. This was true of cow 31, whose liver showed 6.8 parts of arsenic trioxide to the million, or a total of 0.5 grain for the entire organ. It also carried 1.5 grains of copper. Though considerably emaciated, the large quantity of food in the stomach showed that the animal had not lost its appetite, and this was substantiated by the statement of the owner. A sheep from ten miles north of the smelter, on the other hand, though slaughtered, was virtually in a dying condition, and had evidently partaken of but very little food for some time. Only a slight trace of arsenic could be detected in the liver, but a surprisingly large amount of copper was present. Still the animal was undoubtedly suffering from arsenical poisoning, and the reason so little arsenic and so much copper were found is that arsenic is rapidly eliminated while copper is very slowly excreted, being retained mainly by the liver. In some of the cases very large amounts of copper were found in the fat, a part of which had a greenish tinge.

Moderate amounts of arsenic continuously administered, cause an increase in body weight and much increased storage of fat between the muscles as well as around the kidneys. While this is true in general of all animals it is notably true of herbivorous animals. In minute doses arsenic improves the appetite and increases both the motions and secretions of the stomach and duodenum; and since there is no considerable accumulation of arsenic, due to its rapid elimination through the excretory channels, medicinal or smaller doses may be administered daily over a prolonged period without showing harmful effects.

Reliable data on the subject of the arsenical poisoning of live stock are very meagre, and most of the statements found in the usual text books are so conflicting that a definite conclusion as to what may be considered a fatal dose of arsenic for a horse, cow, or sheep, cannot be reached through them alone. Much of the most reliable work has appeared in the chemical journals.

Spallanzani and Zappa[1] fed moderate amounts of arsenic continuously to a "Durham" cow for 46 days, when death resulted. From 0.5 to 3.0 grams (7.7 to 46.3 grains) of arsenious oxide were administered daily, the dose being gradually increased to the maximum of 3 grams, when the animal died. Spallanzani concludes from this and other experiments that cattle will take without injury, over indefinite periods, doses of 0.5 to 0.7 gram (7.7 to 10.8 grains) of arsenic trioxide per day, and may indeed increase in weight under it. They first show toxic symptoms with doses of 1 gram (15.4 grains) per day. The maximum non-toxic dose for cattle is given as about 0.00015 part of arsenious oxide per day for 100 parts body weight, or 10.5 grains per day for an animal weighing 1,000 pounds.

The results cited in the last paragraph are well in accord with the results of the investigations of the writers as made on the animals of smelter districts. A review of the literature of the subject reveals such great discrepancies in regard to the fatal dose that it is almost impossible to believe all of the results cited. On the one hand, we have the work of Cameron[2] which shows that ten cows were killed by one dose for each cow, of 8.4 grains of arsenic trioxide in the form of sodium arsenite. In contrast with this case, which seems to be authentic, we have the statement attributed to Hertwig[3] that he gave arsenic to eight different horses in doses beginning with twenty grains but increasing to a dram, and continued these doses for from 30 to 49 days with no bad effects, in fact, "the condition was improved."

On account of the unsatisfactory state of the literature of this subject, it was decided to inaugurate further experiments to test the effects of

[1] *Annal di Agricoltura*, 131, 25.
[2] *Analyst*, 1888.
[3] *Veterinarian*, 1843, p. 345.

different doses upon cows and horses. However, at this time it was not found possible to meet the expense of such an undertaking, so the work was done upon sheep.

Results of Work on Sheep.—Four of the healthiest sheep were chosen from a flock of several hundred. They were fed upon local arsenic-free hay at Palo Alto, California, and the doses given in starch capsules as follows:

TABLE 3.

	Dose. Arsenic trioxide.	Weight at beginning.	Form of arsenic.
1.	0.181 gram twice a day	95 lbs.	Arsenic trioxide
2.	0.123 gram once a day	87.5 lbs.	Sodium arsenite
3.	0.055 gram once a day	115 lbs.	Sodium arsenite
4.	0.021 or 0.090 gram once a day	90.5 lbs.	Sodium arsenite

The results of this experiment are given graphically in Fig. 1. Sheep No. 4 was given daily doses of 0.021 gram for 35 days, when an increase to 0.090 gram was made, because it was believed that upon the smaller dose the sheep would not die before the conclusion of the experiment at the end of ninety days. This was the only sheep that did not die, but that

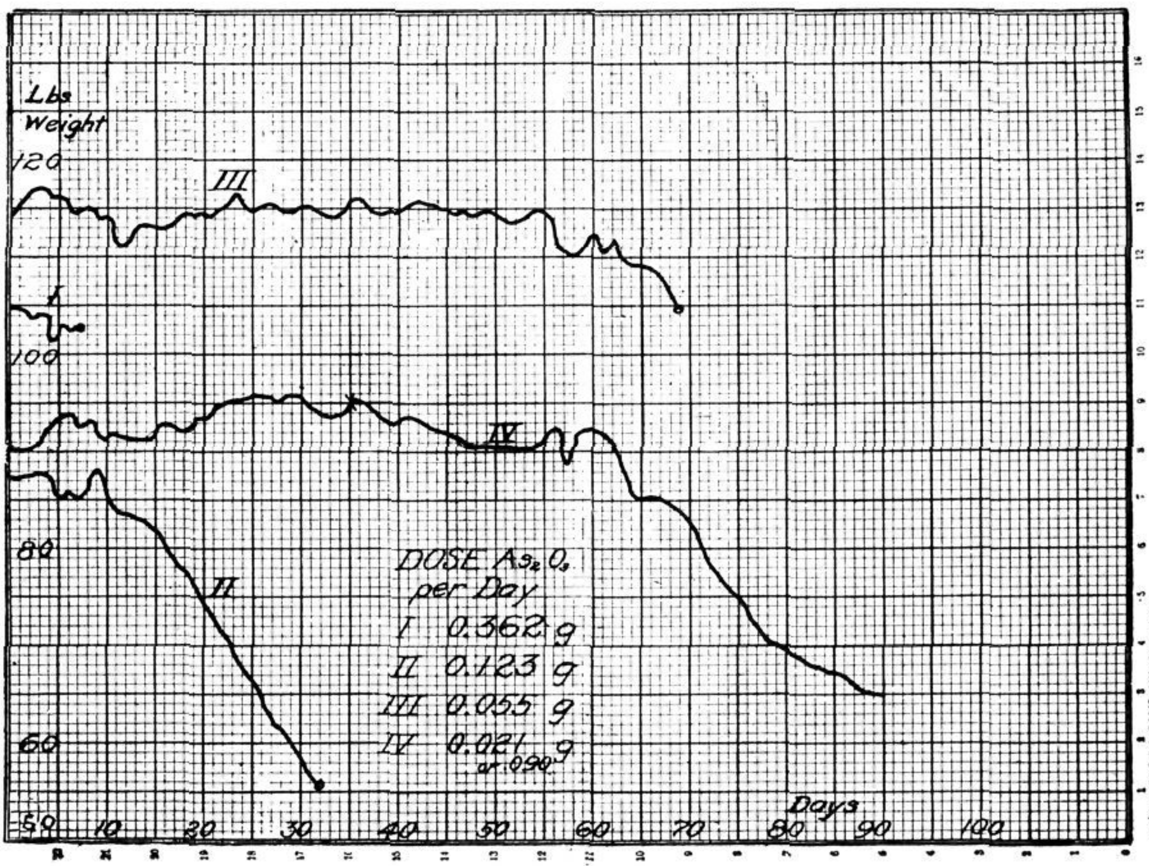

Fig. 1.—Effect of arsenic trioxide on the weight of sheep.

NOTE.—Curve I is raised ten units of weight in order not to interfere with Curve IV.

death would have resulted soon after the expiration of the time set for the close of the experiment is evident from the curve (*IV*) which shows a rapid decrease in weight toward the end of the period.

The experiment shows that 46 milligrams (0.7 grain) of arsenic trioxide per day, administered in the form of arsenite of sodium, to 100 pounds of body weight, is sufficient to cause the death of a sheep. The perfectly regular way in which the arsenic reacted upon the sheep as expressed in the curves of the body weight, at least suggests strongly that the result was not due to individual susceptibility.

The case of sheep No. 2 was an instructive one. It was given a dose of 0.123 gram per day for twenty-five days, and lived eight days longer before death ensued. No food was taken during the last thirteen days, and practically none for eighteen days, though fresh food was offered three times each day. During the eighteen days the animal was practically in a comatose condition, suffering no pain, and reclining upon its side most of the time. On dissection the intestines were found absolutely empty, since an attack of diarrhea had lasted for eight days, while the stomach was greatly distended and packed with solid food. Digestion had been absolutely suspended for a long time, and decomposition of the stomach lining had already begun. At the beginning of the feeding the animal weighed 87.5 pounds, and at the end 56 pounds, of which eight pounds was undigested food packed in the stomach. A number of the doses of arsenic were found undigested in this organ. To each million parts the liver contained a trace, the tissue of the stomach 3.0 parts, and the brain 4.2 parts, certainly a peculiar distribution of the poison. Evidently little arsenic had gone into the circulation from the stomach for a considerable period, so the liver had been able to eliminate most of the arsenic. The post-mortem appearance of the organs of the sheep, taken as a whole, was that of acute rather than long standing chronic arsenical poisoning.

The question of the amount of arsenic which will kill a farm animal, if fed daily, is a very important one to the chemist who undertakes to investigate the conditions existing in smelter regions. The effects depend so greatly upon the conditions that even after such an extensive investigation as that carried out by the veterinarians, pathologists, bacteriologists and chemists, upon the present case, no very definite statements can be made in regard to this point. A study of Table 1 of the second paper of this series will give some idea of the poisonous dose, for on almost all of the ranches listed, animals have been supposed to die from arsenical poisoning. On the other hand, there is almost no place in the farming district where some of the animals will not survive. As has already been indicated, there is comparatively little sickness during the late spring and summer, but by November a large number of animals are affected, if they are allowed to run upon the pastures.

The following table gives the average amounts of arsenic trioxide in the grasses analyzed during the last three years:

TABLE 4.—AVERAGE AMOUNTS OF ARSENIC TRIOXIDE IN GRASS AND HAY.

	As_2O_3 in parts per million.		Grains to 25 pounds food.	
Year.	Grass.	Hay.	Grass.	Hay.
1905	106	45	18.6	7.9
1906	155	42	21.7	7.4
1907	100	..	17.5	...

The column "Grains to 25 pounds food" is supposed to represent the amount of arsenic taken in a day's feeding, since this is the amount of dry matter in the daily ration for this region. On the average, then, the daily ingestion of arsenic is about 20 grains for grass, and 7.5 grains for hay. The amount varies from a minimum of 1.75 grains for young meadow grass taken two miles south of the smelter, to 271.4 grains for a sample taken in the smelter field one fourth mile from the old low stacks. The average for the grass is interesting in comparison with the statement of Spallanzani and Zappa, that one gram (15.4 grains) per day is the minimum amount which can give rise to the toxic symptoms in cattle.

The farmers claim that animals which are shipped into the valley succumb more quickly than those that have lived for some time in the district, and this is undoubtedly true. It might be assumed that this means the animals able to survive are those of great individual resistance and tolerance with respect to arsenic, an assumption which is true in part; but, in addition to this, there is little doubt that tolerance is gradually established to a certain extent by the use of the poison, as is the case with human beings.

In order to see what proportion of the arsenic in the plants would be soluble in the digestive juices of the animals, and thus act as a poison, two digestion experiments were made. A sample of hay or grass, 300 grams, was digested at 38° C. for two days with a glycerol extract of the mucus lining of the abomasum, the mixture being made acid with hydrochloric acid. Then the liquid was made slightly alkaline with sodium carbonate, digested five days with the glycerol extract of two pancreas glands, and toward the end of the time putrefactive bacteria were added. The results were as follows:

	Grass. 5 mi. N.	Hay. 4 mi. N.
Percentage of soluble As_2O_3	0.0242	0.0058
Percentage of insoluble As_2O_3	0.0019	0.00114
Total per cent. As_2O_3	0.0261	0.0069
Percentage of total arsenic which is soluble	92.6	83.6

The greater amount of arsenic is undoubtedly in a poisonous form.

The Distribution of Arsenic in the Organism.—Several animals were sampled in such a way that portions of nearly every organ were taken, but only one set of data will be presented—for a case in which the distribution seemed normal in comparison with our other results, although the amount of arsenic is lower than the average. On November 4, 1906, a horse was killed and sampled. In general condition, the animal was unthrifty, and its coat was very rough. The clinical symptoms were redness in the stomach and intestines, congestion of the lungs and pleura, congestion of the brain and bladder, slight congestion of the kidneys, catarrh of the intestines and an enlarged spleen. The results of the analyses of the organs are presented in Table 5.

TABLE 5.—THE DISTRIBUTION OF ARSENIC IN THE TISSUES OF A HORSE IN A CASE OF CHRONIC POISONING.

No.	Food or organ.	As_2O_3 in parts per million.
1	Grass No. 1	45.00
2	Grass No. 2	107.00
3	Dust from hay	9190.00
4	Ulcer in nose	658.00
5	Contents stomach wet	25.00
6	Contents stomach dried	398.00
7	Urine	59.00
8	Hair of tail	58.00
9	Liver	6.00
10	Thyroid gland	6.00
11	Stomach	4.70
12	Spleen	4.60
13	Pancreas	4.40
14	Small intestines	4.00
15	Brain	3.30
16	Spinal cord	2.60
17	Muscles	2.50
18	Lungs	2.20
19	Bones	2.20
20	Heart	2.10
21	Bladder	1.40
22	Kidney	1.40
23	Right parotid	0.80
24	Fat	0.70
25	Suprarenal	0.06
26	Fluid around heart	0.05
27	Blood	0.03

The horse had fed upon grass and hay containing from twenty to forty-five parts of arsenic trioxide to the million for a period of some months, and for three days had been eating grass containing 107 parts. For several years it had been fed upon grass and hay containing arsenic in varying amounts. Dust shaken from the hay stack in the field where the horses were pastured for three days, contained 9190 parts of arsenic trioxide.

Arsenic in Milk.—Ten samples of milk, most of them mixtures from several cows, were obtained by milking directly into bottles provided with glass stoppers. The analyses gave:

TABLE 6.—ARSENIC IN MILK.

No.	Date, 1906.	Distance from smelter.	No. of cows.	Parts As_2O_3 per million.	Grains to 100 gallons.
1	Sept. 21	4.5 NNE	5	2.94	17.7
2	Nov. 3	5 E	1	0.47	2.83
3	Nov. 3	6 NNE	1	0.70	4.00
4	Nov. 3	4.5 NNE	2	0.18	1.08
5	June 28	4.5 NNE	1	1.40	8.42
6	June 27	5 E	1	1.00	6.02
7	July 2	3 SE	1	4.20	25.28
8	June 28	3 N	5	3.40	20.47
9	June 23	3 W	1	5.70	34.30

The Arsenic Content of Ulcers of the Nose.—A complaint among the horses of smelter regions called the "sore nose" has been observed by the writers in the Anaconda and Salt Lake regions. It is also reported that the same disorder is found in Great Falls, and among the horses of the smelting region in Cornwall. Of the persons who worked on the smelter stacks in determining the arsenic content of the smoke, two became affected with an arsenical rash upon the face, while the nostrils of the third were almost closed by a swelling caused by the irritant action of the flue dust. In the case of horses, one nostril may become closed almost absolutely on account of an ulcer which forms on the lower portion of the nasal partition. Several of these ulcers were taken from the nostrils of different horses and analyzed with the following results:

No.	Distance.	Parts As_2O_3.	No.	Distance.	Parts As_2O_3.
1	2 miles S	254	4	2 miles S	902
2	4.5 miles NNE	587	5	3 miles SW	545
3	3 miles SE	1015			

Undoubtedly the highly arsenical dust from the hay and grass lodges in a fold of the nostril and irritates the mucous membrane until the nose scab is formed. The dust from the hay of the ranch where samples 3 and 5 were obtained, contained 9190 parts of arsenious oxide per million.

In order to see if the cases observed in Salt Lake could be due to this cause, samples were taken in different parts of the district. These samples, taken September 3, 1905, contained from ten to sixty parts of arsenic trioxide to the million, results which would indicate that sufficient arsenic is present to cause the observed effects.[1]

Arsenic in the Hair.—According to the evidence of Mann[2] arsenic is localized in and eliminated by the hair. Large amounts of arsenic were found in the hair of animals of the Anaconda region. The hair of the tail of one horse contained fifty-eight parts of arsenic trioxide to the million, an amount ten times as great as that found in the liver. The hair of a colt contained 605 parts, the liver 4.4 parts, and the bone 13.2 parts, while the

[1] For other results from this district see preceding paper, Table VII.

[2] Report of the Royal Commission, p. 13; and Minutes of Evidence, Vol. 1, p. 139.

grass in the field where the colt was feeding contained only ten parts per million. The hair of a filly pastured five miles north of the smelter gave 460 parts of arsenic. The case is more complicated than those investigated in England, since an unknown fraction of the arsenic in the hair was undoubtedly deposited from the atmosphere. Nevertheless, the results are striking and important.

Normal Arsenic.—Attempts have been made to show that the amounts of arsenic present in the tissues of the animals of smelter regions represent what may be called normal arsenic. This is certainly a perversion of the conclusions of Gautier and Bertrand, for the results obtained by them were of a totally different order of magnitude from those obtained in forensic cases; and they found arsenic only in the thyroid, thymus, brain and skin. Even these results have been criticized by Kunkel,[1] Hödlmoser,[2] Cerny,[3] Stevenson and Mann.[4] The latter writers claim that the arsenic present is wholly adventitious.

No attempt was made by the writers to test Gautier's conclusions, but about forty-five livers from Palo Alto, California, New York City, and Missoula, Montana, were analyzed, using samples of from one hundred to eight hundred grams. Using tests which would detect the presence of 1/1000 mg. of metallic arsenic, in no case was arsenic found. This is sufficient proof that the question of normal arsenic need not come into smelter smoke investigations.

Symptoms.—The following three examples may be taken as typical cases which together exhibit the range of important symptoms which have appeared in connection with arsenical poisoning in the Deer Lodge Valley.

Case (*a*).—The first example is that of a roan mare owned by a farmer living about eight miles north of the smelter. She was eight years old, weighed thirteen hundred pounds, was sleek and fat, and so far as outward appearances went, perfectly sound. The owner stated in answer to questions, that the animal had fed rarely on pasture but almost entirely on hay, of which she ate much more than the average ration. For nearly a year, however, she had been failing in strength, and was no longer able to do an ordinary day's work, profuse perspiration and total exhaustion following any unusual exertion. An examination showed a "sore nose" scar in one nostril.

The animal was shot and the autopsy made immediately thereafter. The urine was white in color and heavily sedimented; the heart "flabby" and larger than normal; the lungs were covered with a mattery adherent exudate and were "flabby," due to the blocking of the bronchii with a

[1] *Z. physiol. Chem.*, **44**, 511–529 (1905).
[2] *Ibid.*, **33**, 329-344 (1901).
[3] *Ibid.*, **34**, 408 (1901).
[4] Minutes of Evidence, Royal Commission on Arsenical Poisoning.

yellow caseous substance, and the escape of air into the tissues; the liver weighed 17 pounds, 7 pounds above normal; the mucous membrane of the stomach was reddened over certain areas in the fundus; the small intestines showed a great many extensive diffuse red patches; the large intestines were generally badly reddened, and here and there distinctly eroded. An unmistakable odor of garlic was observed when the intestines were opened. The mucous membrane of the uterus and bladder was notably reddened, and the right ovary was gorged with a deep red gelatinous substance. The bone marrow was of a deep yellow color, due to a quantity of yellow oil which filled the interstices and retained its liquid character at ordinary temperatures.

Case (*b*).—The second is a colt, one year old, which was posted two miles south of the smelter on July 3, 1906. It began to appear unthrifty during the fall of the preceding year while on the hill pastures, and at no time thereafter did it show a normal growth. The autopsy showed that this was a case of remote chronic rather than of acute poisoning. The secreting mucous membranes throughout the body were reddened in patches, but only slightly. The hair was shaggy and lusterless, and the whole organism weakened and emaciated.

Case (*c*).—The last case is that of a colt, eleven months old, which had developed normally during the sucking period of six months, when it was weaned and removed to an adjoining pasture early in the month of March. From that time until July 1st it subsisted on hay from a stack in the field. On the date mentioned, following an effort to rope it, the colt had a "fit" and died in convulsions. The stomach showed three distinct, crater-like ulcerations and extensively irritated areas, especially in the folds. The lungs were badly discolored as in necrosis or fatty degeneration. The organ was certainly badly affected, and as soft as a partially decomposed organ. The intestines were highly inflamed, often for five to eight inches in one place, and the whole of the small intestine was covered with inflamed patches.

The first of the cases cited is apparently one in which the arsenic showed its usual stimulating action, strengthening the appetite, promoting the digestion, causing the deposition of much intestinal fat and giving a sleek appearance to the subject. The action was proceeding beyond this stage however, and a breaking down of many of the organs was in evidence. This was a case of progressive chronic poisoning, shown further by the large amounts of arsenic in the bone (20.67 parts per million).

The second case seems to be one of true chronic poisoning which evidently took another course, the stimulating effect being constantly overshadowed by the more destructive action of too large doses. The organism was too weak to recover, even after loss of appetite reduced the ingestion of the toxic agent to a minimum. The stomach was nearly empty, and the liver carried only very small amounts of arsenic, while the storehouses for arsenic in the organism, the bone and hair, showed excessive amounts. The analytical results were: hair, 605 parts; bone, 13.2 parts; liver, 3.3 parts; and heart, 1.7 parts of arsenic trioxide per million.

The third case is one of recent chronic poisoning, leading rapidly to a culmination in a way truly characteristic of the substance. The liver of this colt contained 31.7 parts, and the kidneys, 2.4 parts of arsenic trioxide per million.

During a considerable time the writers were associated in this work with Dr. D. E. Salmon, of the Bureau of Animal Industry, who very kindly prepared an outline of the more prominent symptoms of the animals as they appeared to him, for use in this publication. These are given as follows:

Symptoms of the Chronic Arsenical Poisoning caused by the Vegetation of Smelter Regions.

Horses.—1, Raised red line at the base of incisor teeth; 2, breath of a garlic odor; 3, loss of spirit, vigor, and endurance; 4, falling of hair; 5, retention of old hair; 6, ulcers of the nose; 7, weakness and imperceptibility of pulse; 8, erosions on the outer side of gums; 9, puffiness above the eye; 10, rough lusterless hair; 11, partial paralysis of hind limbs; 12, with more acute form: (*a*) Difficult breathing, (*b*) labored action of heart, (*c*) dilation of pupils of the eyes, (*d*) partial paralysis of the diaphragm and costal breathing.

Cattle.—1, Shrinkage of milk within a day or two after smoke has been over pastures; 2, salivation and drooling; 3, constipation; 4, rough scurfy coat; 5, eyes red, inflamed, and weeping; 6, loss of appetite; 7, diarrhea when disease becomes more pronounced; 8, tucked up abdomen; 9, loss of flesh; 10, weakness, loss of vigor; 11, cough; 12, breath of garlic odor; 13, droppings covered with mucus; 14, abortion and failure to breed.[1]

In an examination of the animals of a smelter district the chemist may be greatly aided by a careful post-mortem examination, and by the histological study of small specimens taken for this purpose. The most important features to be seen in the sections taken for microscopical investigation are: proliferation of the connective tissue cells, degeneration and desquamation of the tubules in the kidneys, congestion or diapedesis, the occurrence of hemorrhagic areas, and occasionally a total disintegration of the cells. In some cases there is very marked fatty degeneration. The kidneys show these symptoms more prominently than the other organs.

The Anaconda case is of interest not only to the toxicologist, but also to

[1] The diminution in the human birth-rate was noticed during the Manchester epidemic, and the results tabulated by J. Niven. See Royal Commission on Arsenical Poisoning, Minutes of Evidence, Vol. II, Appendix 17, p. 196.

the industrial chemist and the metallurgist, since arsenic in a great number of cases is a constituent of the metallic sulphides, especially those of copper. Large amounts of arsenic are given off by the smelters of Salt Lake, Utah; Everett, Washington; Great Falls, and Butte, Montana; and from many of the smelters of Germany, England, and other countries. In 1854 and 1875, Haubner investigated the smelter smoke disease in the Freiburg district, and various other cases have been studied to a slight extent.

In the decision of Judge Marshall of the Circuit Court of the United States as made November 5, 1906, the conditions existing in the Salt Lake smelter district are described in such a way as to make an interesting comparison with the results of this series of papers. In speaking of the sulphur dioxide he says: "This gas is heavier than air, and when cooled, falls to the ground at a distance from the smelters dependent upon the air currents. When it is brought in contact with moisture, either in the form of rain, freshly irrigated ground, or the moisture present in growing plants and the foliage of trees, sulphurous or sulphuric acid is formed, which is destructive to vegetation. Besides the emission of gas, some fine dust is emitted from the smelters which contains perceptible quantities of arsenic resulting in the death of horses and cows."

In conclusion, the writers wish to thank Dr. John Maxson Stillman for the many suggestions which have been helpful in this work.

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NOTE ON THE SOLUBILITY PRODUCT.[1]

BY JULIUS STIEGLITZ.

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Nernst[2] was the first to advance the theory that at a given temperature the solubility of a difficultly soluble electrolyte in water or in aqueous solutions of other electrolytes is dependent on a constant called the solubility product, which is proportional to the concentrations of the ions of the salt, each raised to the power corresponding to the number resulting from one molecule. The constant is an important one in the theory of precipitation and solution and particularly useful in calculations of the solubility of a precipitate in mixtures that are not too concentrated. In Nernst's text-book on physical chemistry,[3] the relation for a difficultly soluble binary salt—such as silver acetate—in water and in solutions containing a salt with a common ion, is developed as follows: calling the total concentrations of the difficultly soluble salt m_0 and m in the saturated water solution and in the salt solution respectively,

[1] Reported at the Chicago meeting of the American Chemical Society.
[2] *Z. physik. Chem.*, 4, 372 (1889).
[3] Translation of the 4th German Edition (1904), p. 527.