STUDIES IN IODINE METABOLISM

L. Van Middlesworth

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Memphis, Tennessee 38163

RESEARCH CONTRACT NO. DE-AS05-76EV01643

Progress Report

and

Publications

1979-1980

DISCLAIMER

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PROGRESS REPORT, 1979-1980

I. Environmental Monitoring:

Much of the positive data of the present two years are summarized in the attached manuscript, entitled "Small quantities of ^{131}I in thyroids of sheep from Wales". We have observed no new increments of ^{131}I in animal thyroids from June, 1979, to June, 1980. We have expanded our sources of animal thyroids in this country, and we have monitored sheep from Brownwood, Texas, and cattle from Mississippi, Alabama, South Carolina, Georgia, Florida, Tennessee, and cattle from Arkansas transported to Tennessee for slaughter. However, we have not received thyroids specifically from Arkansas; I was informed by the Arkansas Department of Health that that department monitors thyroid glands in the state of Arkansas. We have observed no new ^{131}I in animal thyroids from the United States or from other countries since May, 1979; but we have continued to monitor 5-20 thyroid glands every 1-3 weeks from Japan, New Zealand, Australia, West Germany, England, and Canada.

Last year, when an orbiting satellite (VELA) detected an artifact in the southern hemisphere on September 22, 1979, we were sampling thyroids from sheep in New Zealand and Australia. Our samples from October 22, November 5, and November 12, 1979, showed no measurable quantities of ^{131}I. The samples from October 22 were delayed in the mail for 20 days, and that would have reduced their importance. Gamma spectra were determined on all these specimens, but no measurable ^{131}I was found. The minimum detectable quantity was 0.6 to 1 pCi $^{131}I/g$ (depending upon the transit time in the mail).

Each week, we also monitor 3-5 human thyroids from the Tennessee State Medical Examiner's Office. These glands are studied as part of the autopsy report of accidental deaths. During the past year, we have studied 140 thyroids, and radioactivity was detected in only one gland. That radioactive thyroid was from a man who had been studied with Tc-99m eleven months before his accidental death. It is assumed that this radioactivity was a small quantity of long-lived contaminant which was present in the technicium 99M; however, I was unable to identify the source of activity, and the sample was forwarded to Dr. Richard B. Holtzman at Argonne National Laboratory for possible identification of the radioactive contaminant. Dr. Holtzman will also test the gland for possible alpha emitters.

II. Radium in Cattle Thyroids:

Radium has been present, as previuosly reported by this laboratory, in more than 50% of the thyroids from old milk cows slaughtered in the Memphis area. Recently, we have found radium in cattle thyroids from Georgia, Alabama, and especially those from Mississippi. After we observed radium in thyroids from New Zealand cattle, we notified our corespondent in New Zealand, Dr. Batt, of Massey University. Dr. Batt suggested that a source of the radium in the cattle glands may be the large quantitites of superphosphate fertilizer currently used in New Zealand.

III. Relationship of Thyroid Function to Seizures in Rats:

Two years ago, studies within this project showed that offspring of rats maintained on low-iodine diet were sensitive to audiogenic seizures (Endocri-

nology, 1977; Endocrinology, June, 1980). During the past year, we have shown that 85-90% of offspring of rats fed $KClO_4$ or KSCN (to compete with iodide metabolism) frequently had no apparent sensitivity to audiogenic seizures; yet, if these animals were made hypothyroid as adults, they were sensitive to audiogenic seizures; and these seizures could be prevented or masked by replacement doses of thyroxine. Yet, if the thyroxine treatment was stopped and the animals again made hypothyroid, then the sensitivity to audiogenic seizures returned. Less than 2% of control animals developed audiogenic seizures, regardless of their thyroid status. Therefore, neonatal iodine deprivation resulted in adults with a masked sensitivity to audiogenic seizures; however, in these animals, the seizures were not observed unless the animals were made hypothyroid. These experiments prove that iodine depletion caused a CNS abnormality which may not be reversed by thyroxine treatment, but can be completely masked by thyroxine treatment, using only the normal maintenance dose of T_4.

IV. The Effect of KSCN upon Thyroglobulin in Mice:

Previously, we have shown that KSCN fed to mice caused iodine to accumulate in their thyroid glands in a form which could not be released. We have followed residual radioactivity in a group of these mice for more than one year, and the animals fed KSCN contained eight times more of the residual iodine than controls.

During the past year, we have repeated these studies, using nonradioactive diets, and chemical iodine analysis on the thyroids. This was to evaluate the possible role of the ^{125}I-labelled diet in producing residual iodine in the thyroid glands. Two groups of mice were fed low-iodine diet, one of which contained 300 micrograms of KSCN per kg of diet, and the controls only low-iodine diet. After three months, the animals fed the KSCN contained four times more iodine in their thyroid glands than the controls. These experiments prove that the previous experiments in which labelled diets were used were just as valid as experiments in which no radioactivity was fed. Therefore, the accumulation of unavailable iodine in the thyroid gland was not caused by radiation damage to the thyroid glands, but by the KSCN in the diet.

V. Studies on Excessive Iodide Intake:

Previously, we have confirmed the results of Arrington et al. (J. Nutrition 87: 394, 1965) regarding the lethal effect of high iodide intake on neonatal rats. Last year, we further investigated this problem, and we studied the effect of high iodide intake on the motility and excitability of the colon and of the uterus. In addition, we measured the serum iodide concentration in the dams and in the fetuses, and in the few pups which were born alive.

We found that the uterus was insensitive to oxytocin and the colon had reduced motility in the presence of 35 micromolar concentration iodide in the serum. The fetuses and newborn rats contained 30% higher iodide concentration than their dams. Therefore, high iodide intake of the pregnant or nursing rat resulted in exaggerated concentrations of iodide in the fetus and the offspring.

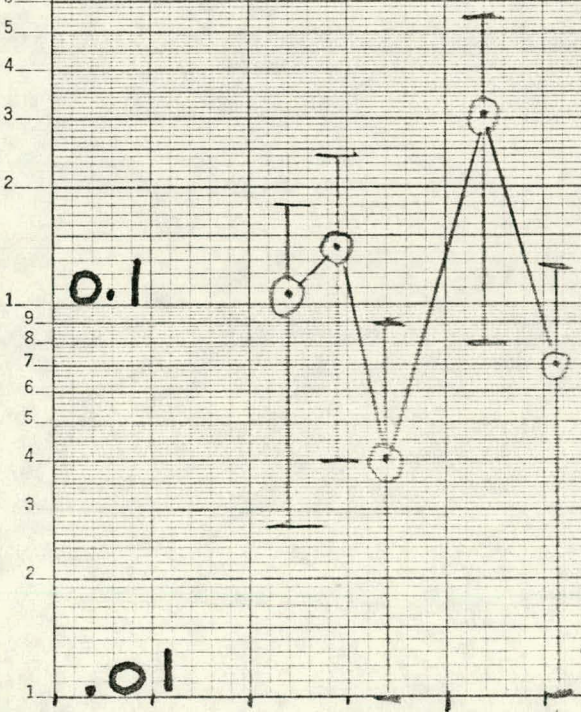
Alabama Cattle
Long-Life Radioactivity
0.3-0.4 MEV

I = range

⊙ = mean

→1980

c/m/g



Augusta, Georgia Cattle

Long-Life Radioactivity

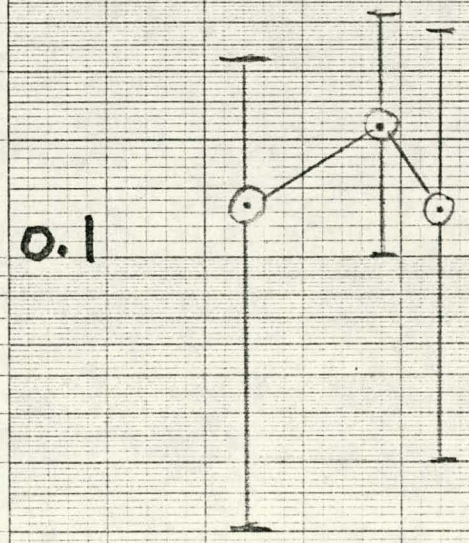
0.3 - 0.4 MEV.

→1980

c/m/g

I = range

⊙ = mean



1.0

0.1

.01

AP 15 MAY 15 JE 15 JI

1980

Mississippi Cattle

LONG-LIFE RADIOACTIVITY
0.3-0.4 MEV.

→ 1980

I = RANGE

⊙ = MEAN.

c/m/g

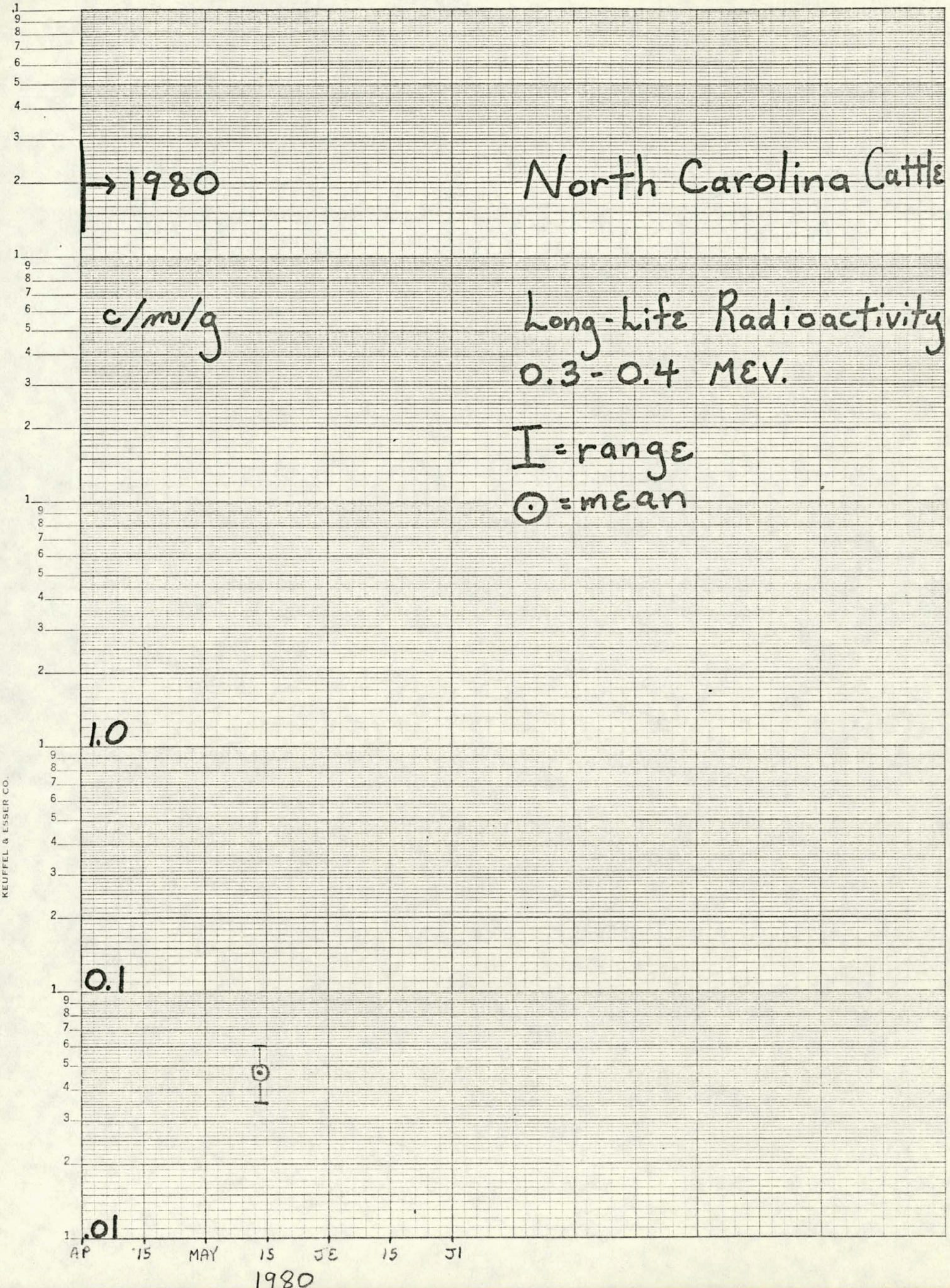
1.0

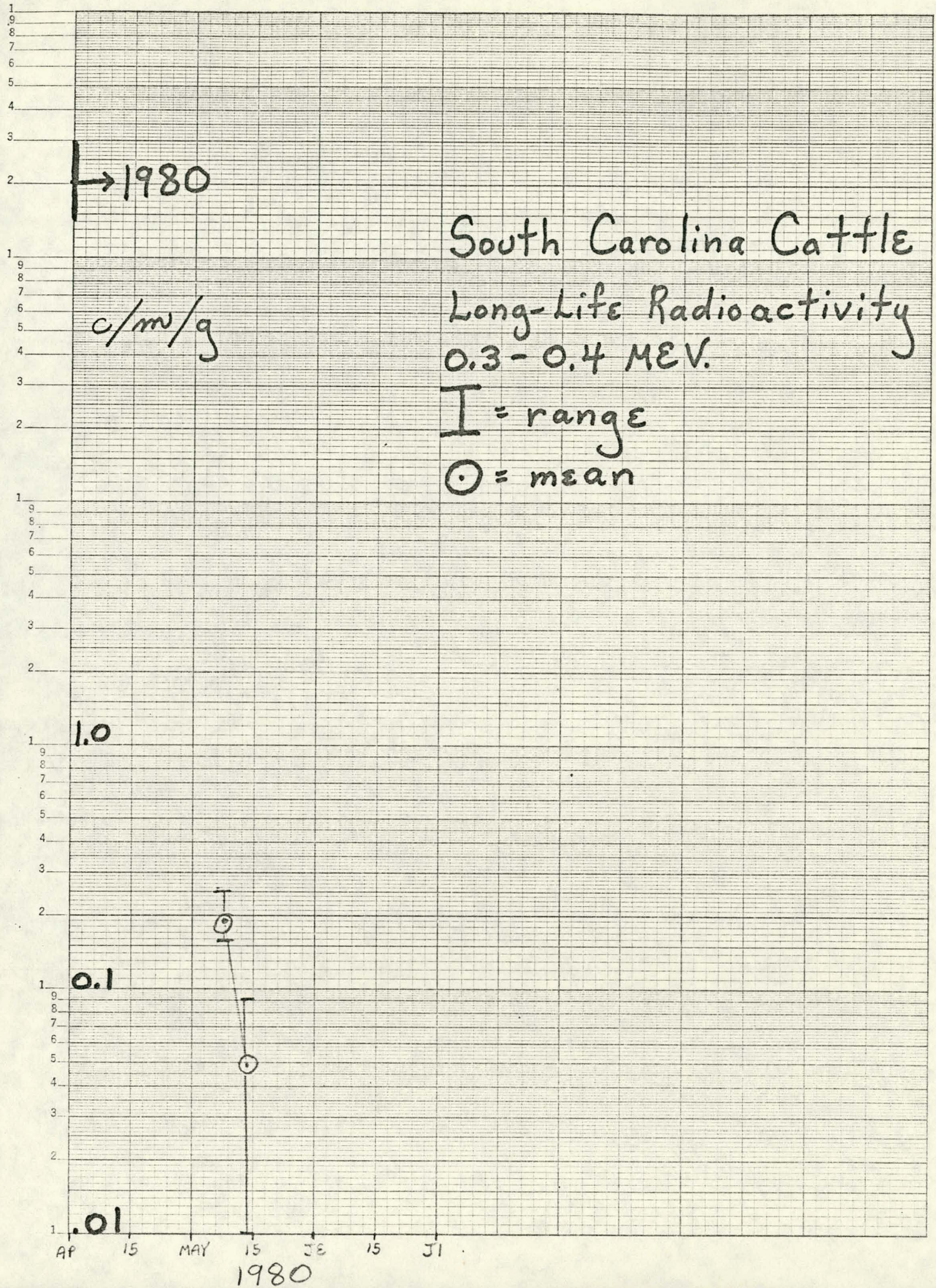
0.1

.01

AP 15 MAY 15 JUN 15

1980


North Carolina Cattle
Long-Life Radioactivity
0.3 - 0.4 MEV.
I = range
⊙ = mean
→1980
c/mu/g
1.0
0.1
.01
AP
15
MAY
15
JE
15
JI
1980


→1980
South Carolina Cattle
Long-Life Radioactivity
0.3 - 0.4 MEV.
I = range
⊙ = mean
c/m/g
1.0
0.1
.01
AP
15
MAY
15
JE
15
JI
1980

Florida Cattle
Long-Life Radioactivity
0.3 - 0.4 MEV.

I = range

⊙ = mean

→ 1980

c/m/g

1.0

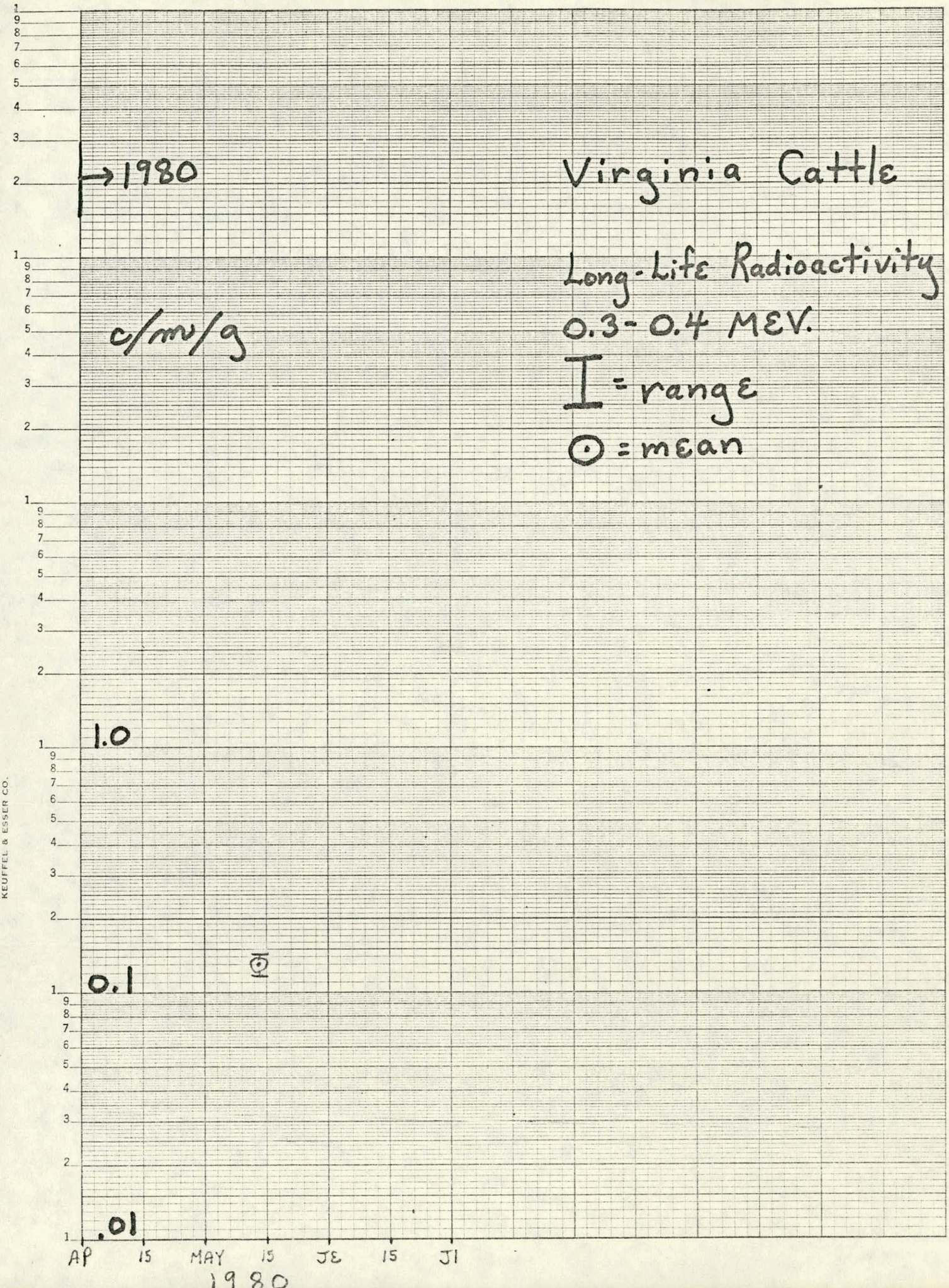
0.1

.01

AP 15 MAY 15 JE 15 JI

1980

KEUFFEL & ESSER CO.


→1980
Virginia Cattle
Long-Life Radioactivity
0.3-0.4 MEV.
I = range
⊙ = mean
c/m/g
1.0
0.1
.01
AP
15
MAY
15
JE
15
JI
1980
KEUFFEL & ESSER CO.

MEMPHIS CATTLE

LONG-LIFE RADIOACTIVITY

C/m/g

⊙ MEAN

I = RANGE

I = S.D.

1.0

0.1

0.01

April 15 | May 15 | June 15 | JULY | AUG | SEPT | OCT | Nov | DEC | JAN | FEB | MAR | APR

1980

.0 pCi ^{131}I/gm

00 Texas Sheep

6

0

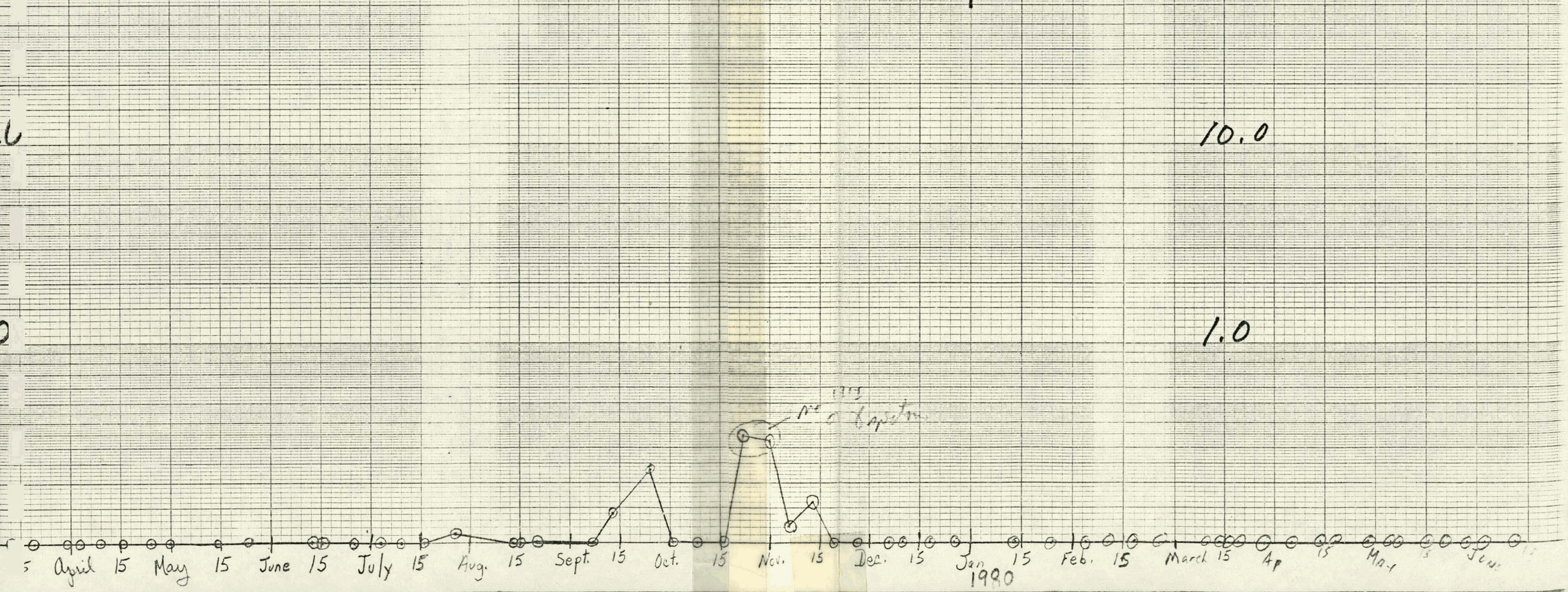
1000.0 pCi ^{131}I/gm

Texas Sheep

→ 1980

10.0

1.0



.J pCi ^{131}I/gm

1000.0 pCi ^{131}I/gm

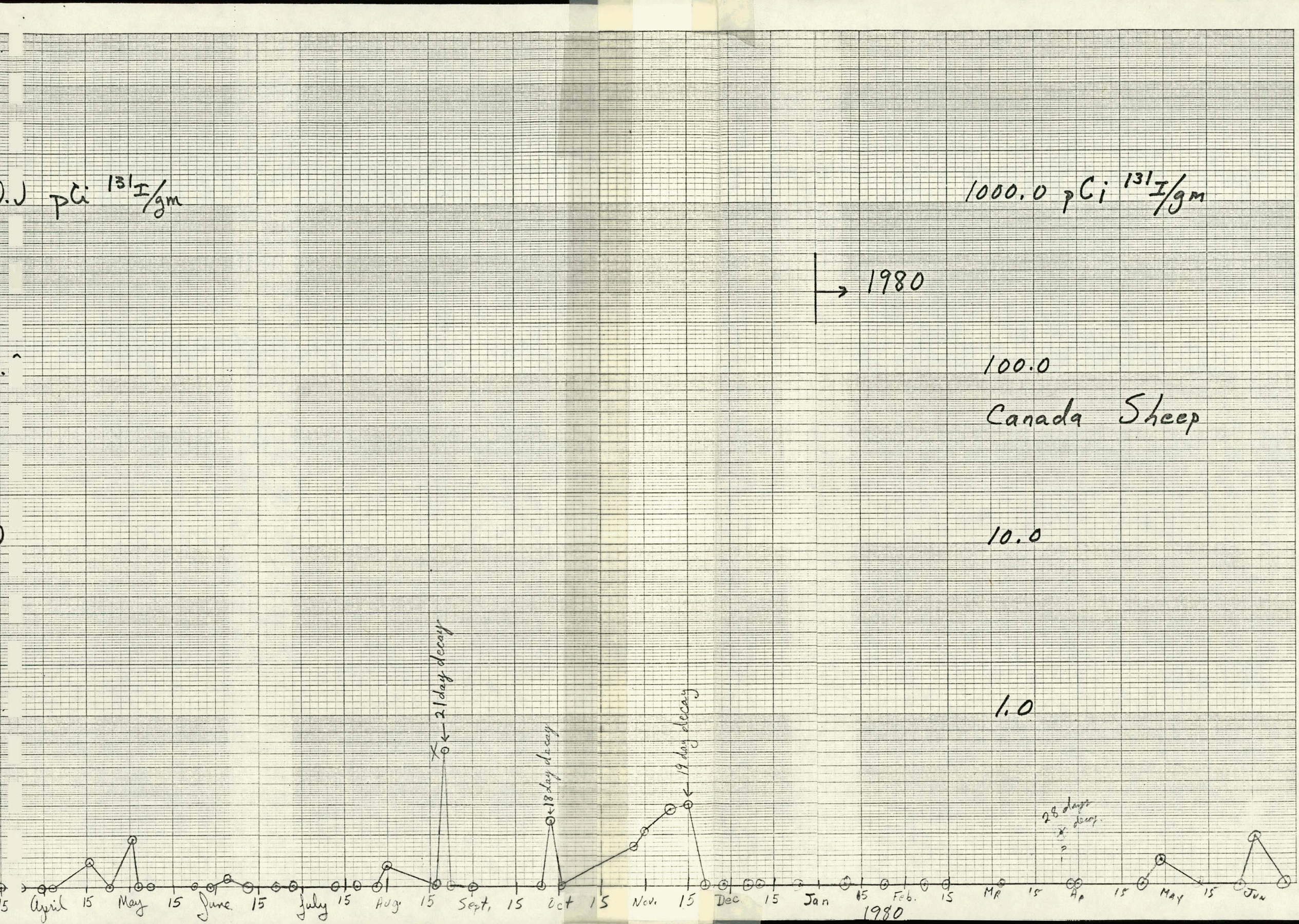
→ 1980

100.0

Canada Sheep

10.0

1.0



)00.0 pCi ^{131}I/gm

1)0.0

1J.0

0

1980

England

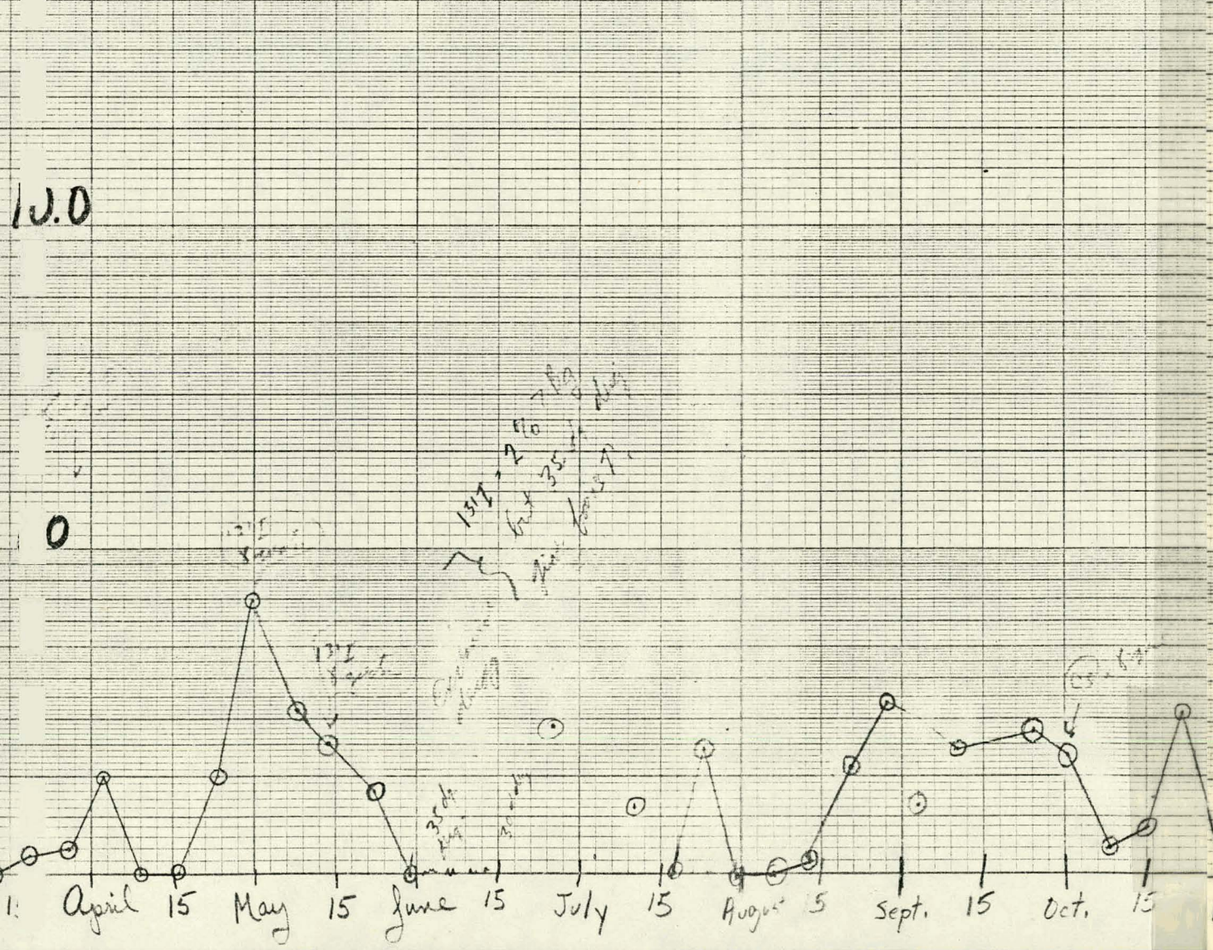
Sheep

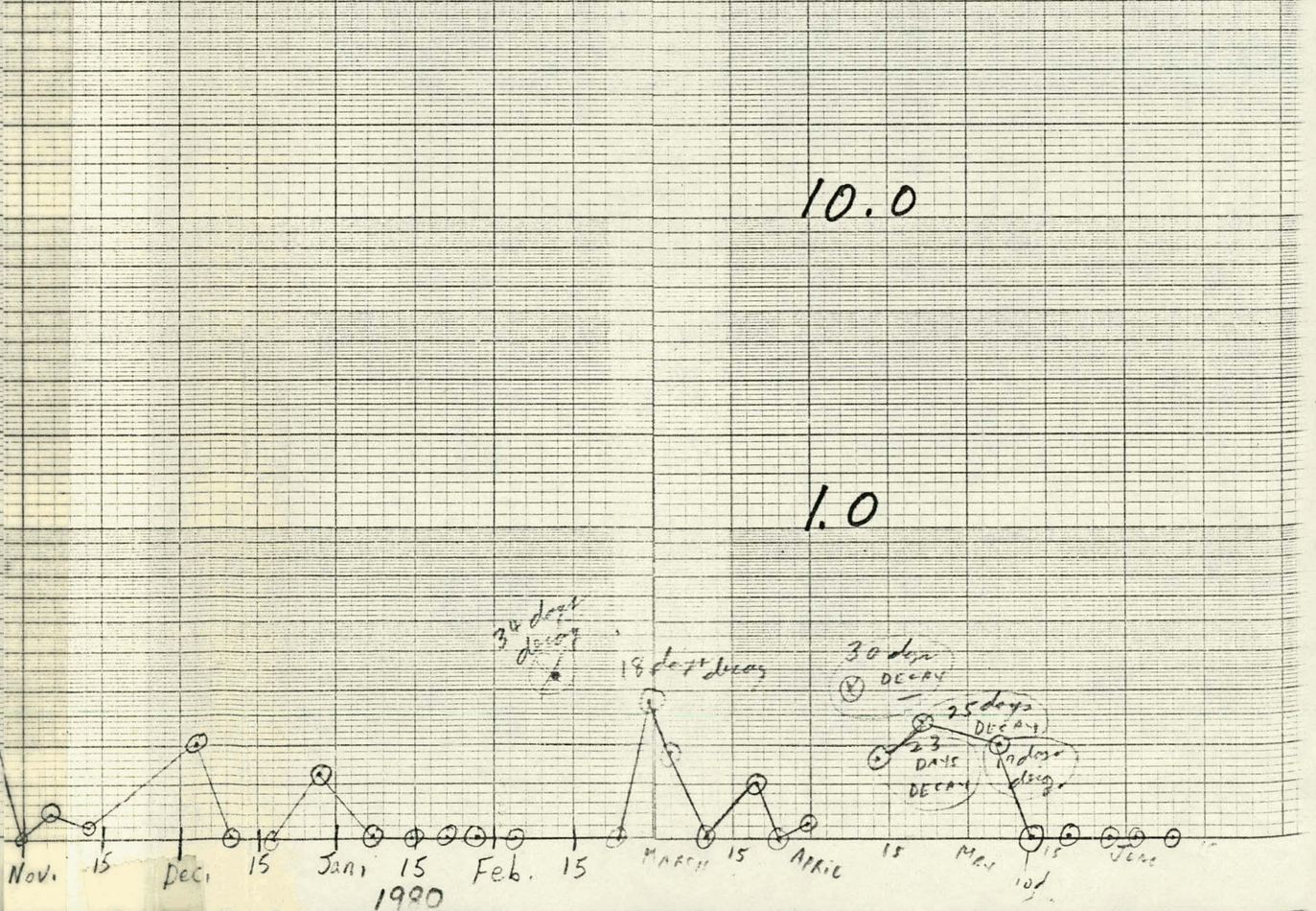
1000.0 pCi ^{131}I/gm

100.0

10.0

1.0



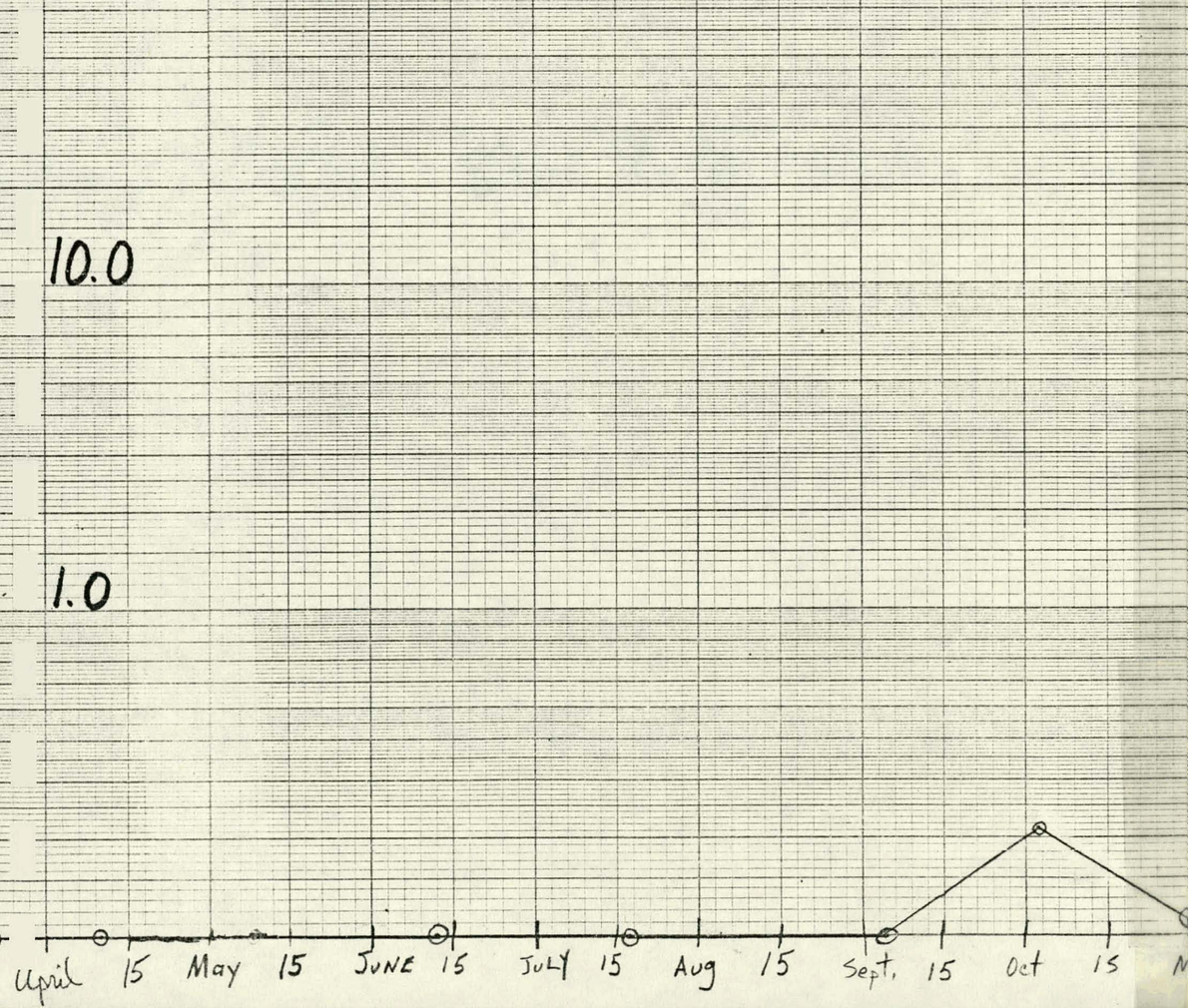


1000.0 pCi ^{131}I/g

100.0

10.0

1.0



→ 1980

1000.0 pCi ^{131}I/gm

Ulm Cattle

West Germany 100.0

10.0

1.0

1000.0 pCi ^{131}I/gm

100.0

10.0

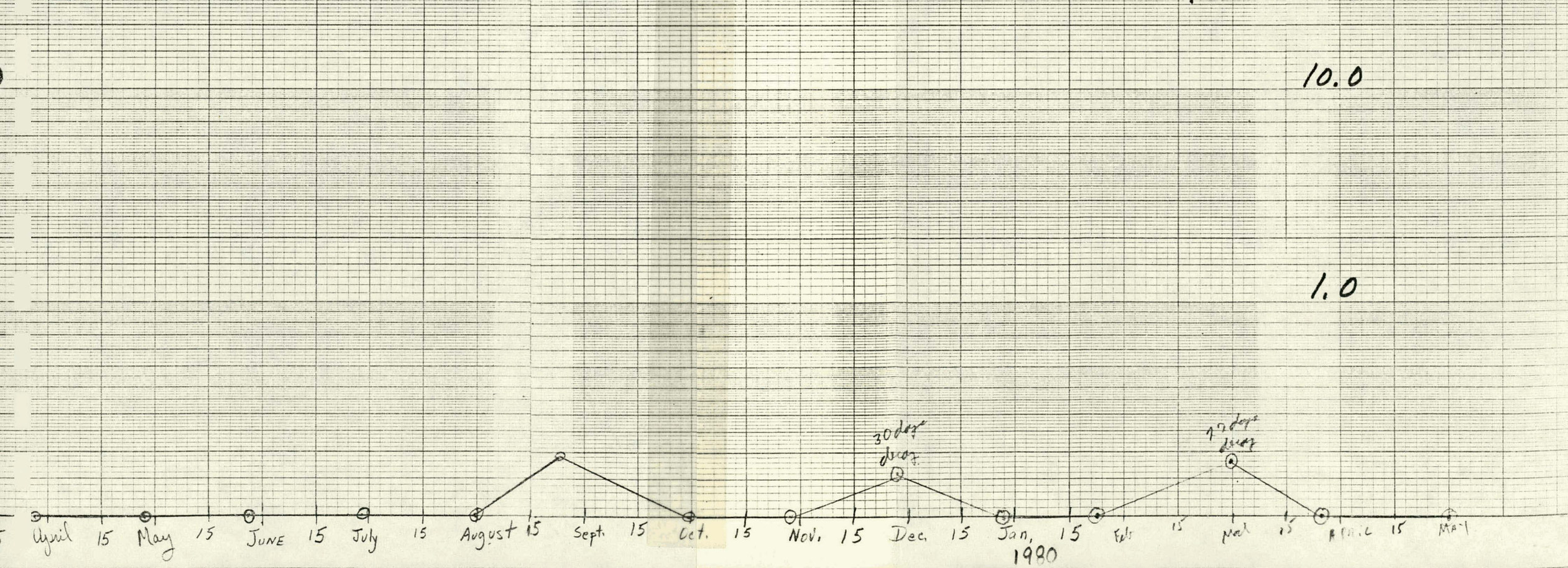
1.0

0.1 pCi ^{131}I/gm

0

→ 1980

Japan Cattle



1000.0

100.0 pCi ^{131}I/gm

10.0

1.0

12 day 9 day 14 day 12.7 day decay

5 April 15 May 15 JUNE 15

11 day 19 day decay 11 day decay 8 day decay 21 day decay (400 mR)

July 15 Aug. 15 Sept. 15 Oct. 15

UNDEPENDABLE MARC 1979-80

Australia
Sheep
→1980

7 day decay 16 day decay

SPECTRUM 1000 MR SHOWED NOTHING

LOST IN MARC

Nov. 15 Dec. 15 Jan. 15 Feb 15 MARCH 15 Ap 15 May 15 JUN 15

1980

1000.0

100.0 pCi ^{131}I/gm

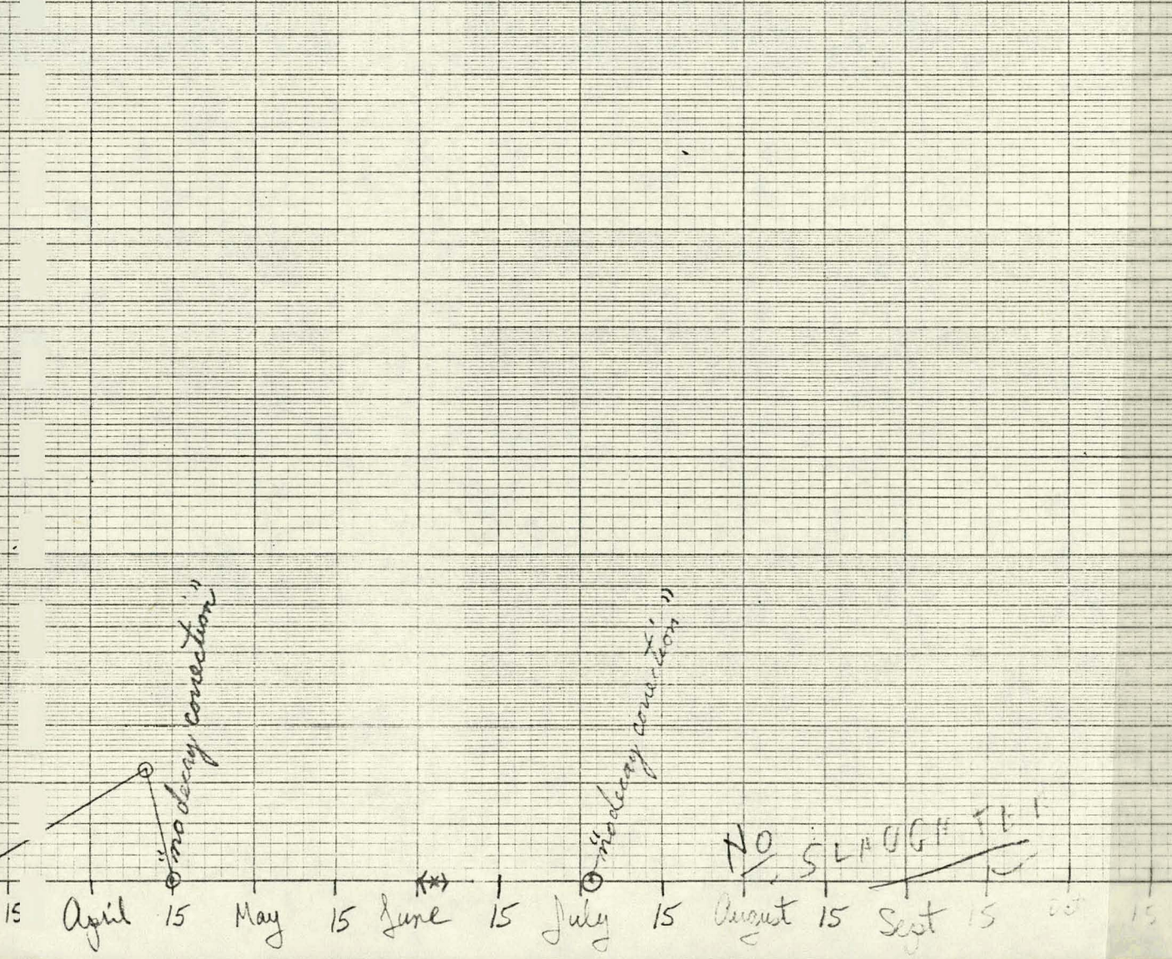
10.0

1.0

15d day

19d day

Zealand Cattle



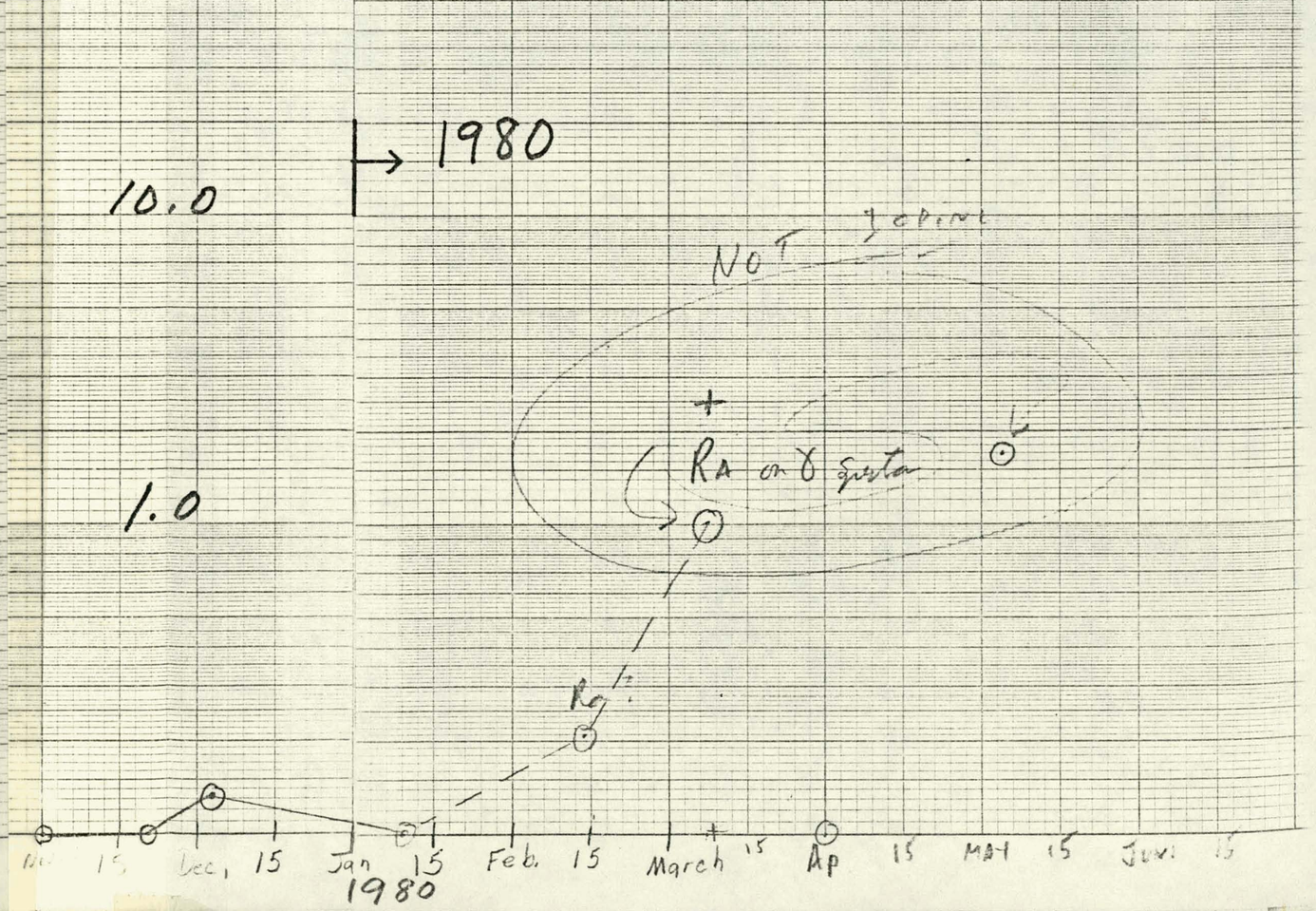
pCi ^{131}I/gm

100.0

10.0

1.0

New Zealand Cattle



...e-land Sheep

April 15 May 15 June

"no heavy snowfall"

July 15 August 15 Sept 15 Oct. 15

"no heavy snowfall"

pCi ^{131}I/gm

100.0 New Zealand Sheep

10.0 → 1980

1.0

Nov. 15 Dec. 15 Jan. 15 Feb. 15 MARCH 15 AP 15 May 15 June 15

1980

PART IV

TABLE 1: DEATH OF OFFSPRING OF PREGNANT RATS FED A 0.13% POTASSIUM IODIDE SOLUTION.

DAYS OF KI FEEDING BEFORE PARTUITION DATE	NUMBER OF DAMS	PUPS DELIVERED	PUPS UNDELIVERED	PER CENT DELIVERED	PER CENT OF PUPS SURVIVING 2 DAYS	PER CENT OF PUPS SURVIVING 7 DAYS
0 (CONTROLS)	5	53	0	100	83	83
2	2	18	0	100	44	44
4	3	30	1	97	7	0
5	6	50	16	76	10	0
6	4	20	29	41	5	0
≥ 7	2	5	20	25	0	0

TABLE 2: PLASMA IODIDE CONCENTRATIONS OF RATS GIVEN A 0.13% KI SOLUTION AS DRINKING WATER (LABELED WITH I^{125}) FOR 40 DAYS.

NUMBER OF RATS	MEAN PLASMA IODIDE CONCENTRATION			
	μM	S.D.	μG%	S.D.
11	35	8.9	4480	1100

THE PLASMA IODIDE CONCENTRATION IN NORMAL RATS NOT FED EXCESSIVE KI VARIES FROM ABOUT 0.1 μG% TO 2.0 μG%.

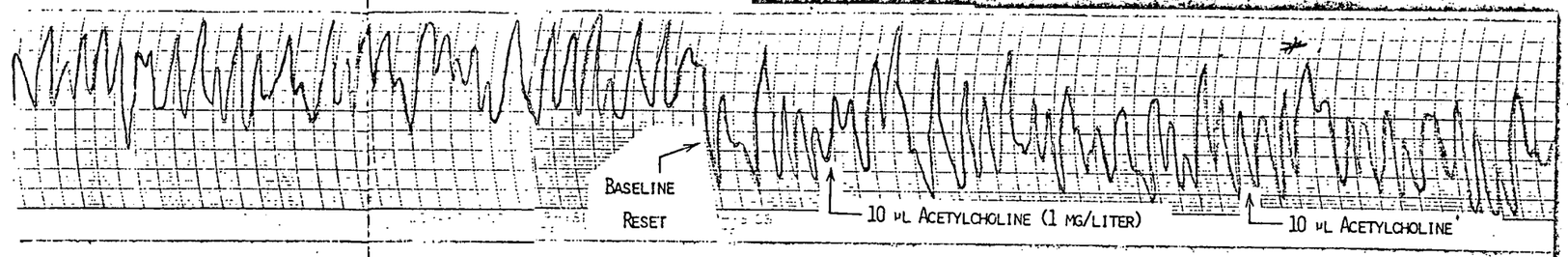
TABLE 3: PLASMA T_4 OF RATS GIVEN 0.13% KI SOLUTION AS DRINKING WATER FOR 40 DAYS.

RATS	NUMBER	MEAN T_4 µG%	S.D.
CONTROLS	15	3.81	0.99
KI FED	13	3.62	1.52

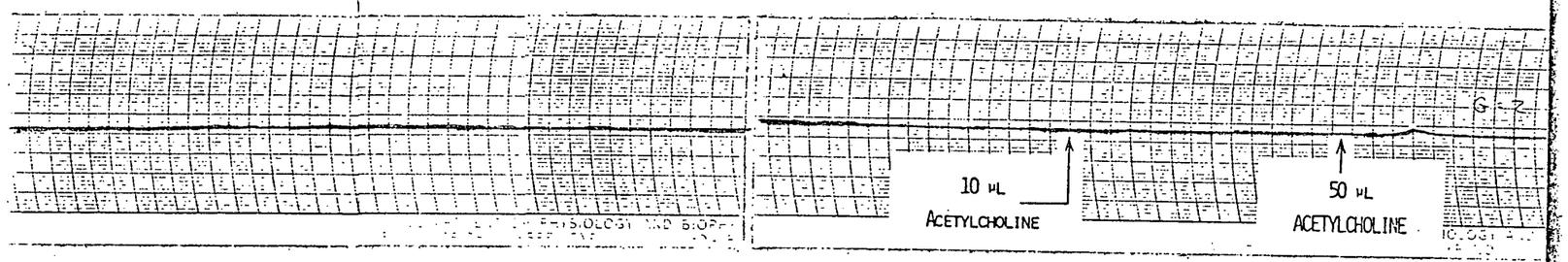
1 OF 13 RATS FED KI FOR 40 DAYS HAD A T_4 < 1 µG% (NORMAL RANGE IS 1 TO 5 µG%).

COLON

CONTROL

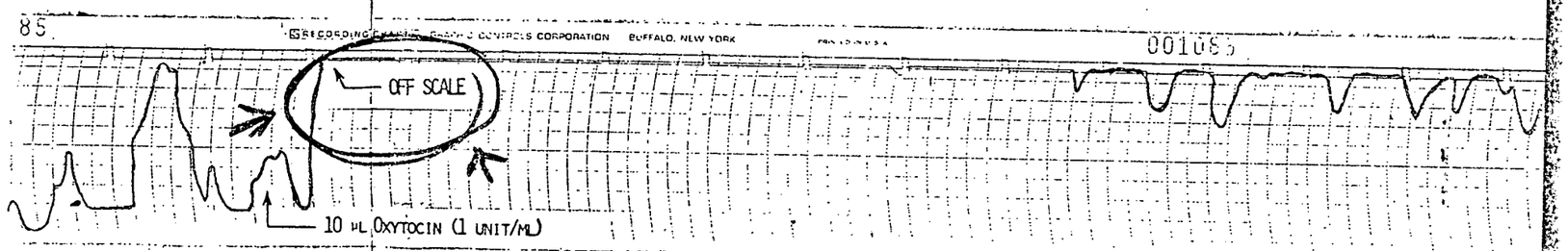


KI

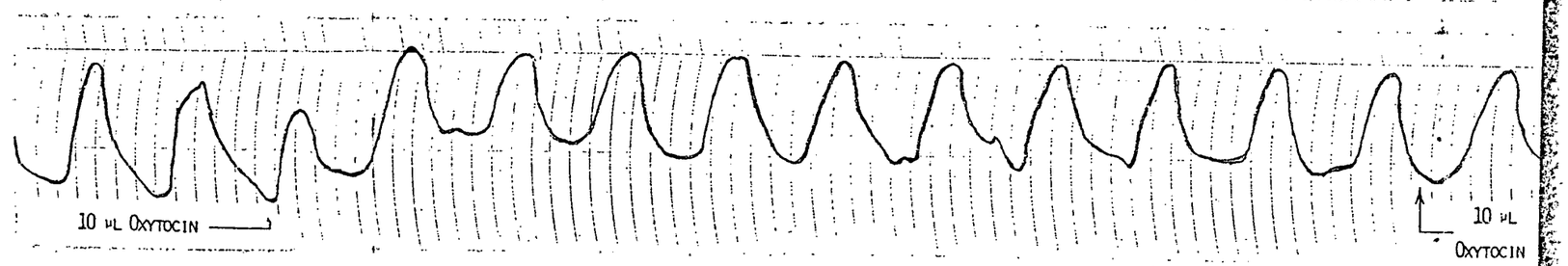


UTERUS AT TERM

CONTROL



KI



PART IV

SMOOTH MUSCLE MOTICITY

PUBLICATIONS, 1979-1980

Reviews

1. Goodman, H. M.,and L. Van Middlesworth. The thyroid gland. In: Medical Physiology, 14th edition. Ed. V. B. Mountcastle. Mosby Press, 1980.

In press

2. Van Middlesworth, L. The pituitary-thyroid relationship in pregnancy. In: Endocrinology of Pregnancy. Ed. J. R. Givens. Year Book Publishers, 1980.

3. Van Middlesworth, L. Thyroid disease in pregnancy. In: Endocrinology of Pregnancy. Ed. J. R. Givens. Year Book PUblishers, 1980.

Original investigation

4. Van Middlesworth, L., and C. H. Norris. Audiogenic seizures and cochlear damage in rats after perinatal antithyroid treatment. Endocrinology 106: 1686-1690, 1980.

Submitted for publication

5. Van Middlesworth, L. Small quantities of ^{131}I in thyroids of sheep from Wales. Submitted June 6, 1980.

Abstracts

6. Mullen, S. P., S. J. Schaeffer, R. D. Howell, and L. Van Middlesworth. Smooth muscle paralysis from iodide feeding. Fed. Proc. 30, Abst. 2364, 1980.

7. Van Middlesworth, L., Mullen, S., and Schaeffer, S. Lethal effects of iodide in pregnancy. Clin. Res. (Southern Soc. for Clin. Invest.), January, 1980.

8. Kato, N., V. Havlicek, and L. Van Middlesworth. Immunoreactive somatostatin (IRS) levels in brain regions of normal vs. neonatally thyroid-deficient rats susceptible to audiogenic seizures. The Endocrine Soc. Program, Abst. 112, June, 1980.

9. Sundwark, V. C., V. Havlicek, and L. Van Middlesworth. β-endorphin levels in brain regions of normal vs. neonatally thyroid-deficient rats susceptible to audiogenic seziures. The Endocrine Soc. Program, Abst. 115, June, 1980.

10. Van Middlesworth, L. Antiseizure effect of thyroid hormones. Submitted to Program of Am. Thyroid Assoc., 1980.

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