EFFECTS OF SUB-LETHAL DOSES OF UREA ON PREGNANT CATTLE

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Summary

Six pregnant cows received, by injection into the rumen, 0.20 to 0.30 g urea/kg body-weight at 104 to 148 days of pregnancy, 0.35 g/kg at 124 to 169 days of pregnancy, 0.35 g/kg at 208 to 226 days of pregnancy and 0.30 g/kg at 256 to 273 days of pregnancy. The change in blood ammonia concentration was followed for approximately seven hours after dosing.

Five cows survived until calving and gave birth to healthy calves after gestation periods of 281 to 287 days. Thus, it appears that sudden access to a high intake of urea is unlikely to result in abortion or stillbirths.

One cow receiving 0.35 g/kg at 208 days of pregnancy and a further two non-pregnant cows receiving 0.40 g and 0.45 g/kg under the same experimental conditions died from urea toxicity.

In cows receiving non-fatal doses of 0.20, 0.25, 0.30 and 0.35 g urea/kg, the mean maximum increases of blood ammonia-nitrogen concentration were 3.1, 3.4, 6.1 and 6.0 μg/ml respectively. The three animals receiving fatal doses of 0.35, 0.40 and 0.45 g/kg had maximum blood ammonia-nitrogen increases of 27.1, 22.0 and 19.5 μg/ml at the final samplings 60, 13 and 15 min before death respectively.

I. INTRODUCTION

During recent years there has been a considerable increase in the supplementation of grazing cattle with feedstuffs containing urea, particularly those provided in the block form. Associated with this increase in usage, there have been occasional reports of suspected abortion and/or stillbirths in cattle. As cattle in Queensland are grazed under extensive conditions, there is often little differentiation between pre- and post-natal wastage, and these reports have been either not well authenticated or other possible causes have not been eliminated.

In view of the reports it was desirable to examine experimentally the possibility that dietary urea adversely affected the bovine foetus. It was considered that if abortions or stillbirths resulted, they would be associated with the intake of a near-fatal dose of urea, as could occur with group supplementation.

This paper records the results of studies on the dosing of pregnant cattle with urea. As Dinning *et al.* (1948) and Repp *et al.* (1955) showed that elevated blood ammonia values were associated with urea toxicity, determinations of this constituent were made at each dosing.

II. MATERIALS AND METHODS

(a) Animals

Six Hereford cows were used in the main study. These animals were between 104 and 148 days pregnant and varied in body-weight from 323 to 445 kg at the start of the experiment.

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Two non-pregnant Hereford cows with body-weights of 376 kg and 415 kg were used to determine the fatal dose of urea under the conditions of the experiment.

(b) Animal Management

The animals were housed in individual stalls and each received daily a ration of *Paspalum dilatatum* chaff ***ad libitum*** (4.7% crude protein in dry matter) supplemented with 1.4 kg lucerne chaff (17.4% crude protein in dry matter).

On the days that urea was administered to the experimental animals, they were removed from the stalls at 0700 h and the urea was injected 1.5 to 2.0 h later. Neither feed nor water was available from 0700 until 1700 h, when the animals were -returned to the stalls.

The cows were weighed between 0700 and 0800 h on the day prior to dosing and the calves were weighed within 16 h of birth.

(c) Administration of Urea

The calculated dose of urea was dissolved in one litre of distilled water and injected into the rumen with a 23 cm needle.

The two non-pregnant cattle received 0.40 g/kg (total dose 146.8 g) and 0.45 g/kg (total dose 186.8 g) urea to determine whether, under the conditions of the experiment, these dose rates resulted in death. As these amounts proved fatal, the six pregnant animals received doses varying from 0.20 to 0.30 g/kg at the first series of observations. Because no clinical signs of urea toxicity were observed at these levels, the doses for the second and third series were increased to 0.35 g/kg. One animal succumbed to urea toxicity during the third series, so the dose was reduced to 0.30 g/kg for the fourth observation made in late pregnancy. The body-weight, dose rate of urea and the stage of pregnancy at each of the observations are given in Table 1.

(d) Blood Ammonia Determinations

Duplicate samples of jugular blood for blood ammonia determinations were obtained prior to administration of urea, at approximately 30 min intervals for the next 4 h and then at approximately 60 min intervals for a further 3 h.

A 2 ml syringe was used to obtain blood from the jugular vein and the 2 ml sample was transferred immediately to a test tube containing 2 ml of cold 20% (w/v) trichloracetic acid. The test tubes were kept in a container of ice then centrifuged at approximately -5 °C within 60 min of sampling. One ml of supematant was pipetted into a 25 ml bottle containing 1 ml of 40% potastium hydroxide and the ammonia was diffused and determined as described by Seligson and Seligson (1951). Satisfactory recoveries of ammonia were obtained from trichloracetic acid solutions and from blood using either saturated potassium carbonate or 40% potassium hydroxide. However, subsequent results showed that potassium hydroxide gave higher basal values than potassium carbonate apparently due to breakdown of nitrogenous compounds not precipitated by the trichloracetic acid. For this reason basal values prior to treatment have been subtracted from values after treatment.

On each of six days during the third series of observations, one of the six experimental cows received urea and another received one litre of distilled water by injection into the rumen. This allowed a study of diurnal changes in blood ammonia in untreated animals under the conditions of the experiment. Thus;

TABLE 1

Schedule of ruminal dosing of urea, showing body-weight of cows and stage of pregnancy

Animal No.	Series 1			Series 2			Series 3			Series 4		
	Stage of Pregnancy (days)	Body-weight (kg)	Dose Rate (g/kg)	Stage of Pregnancy (days)	Body-weight (kg)	Dose Rate (g/kg)	Stage of Pregnancy (days)	Body-weight (kg)	Dose Rate (g/kg)	Stage of Pregnancy (days)	Body-weight (kg)	Dose Rate (g/kg)
1	127	435	0.2	164	404	0.35	218	451	0.35	262	446	0.3
2	104	443	0.2	124	440	0.35	*208	445	0.35	—	—	—
3	115	365	0.25	141	362	0.35	212	375	0.35	256	355	0.3
4	128	445	0.25	152	455	0.35	226	475	0.35	266	474	0.3
5	—	—	—	144	323	0.35	223	373	0.35	270	350	0.3
6	148	395	0.3	169	395	0.35	225	408	0.35	273	398	0.3

*Animal No. 2 died from urea toxicity 3 h after dosing.

during the experiment results on blood ammonia were available on 6 animals not receiving urea, and for 2, 2, 6, 12, 1 and 1 animals receiving 0.20, 0.25, 0.30, 0.35, 0.40 and 0.45 g urea/kg respectively.

III. RESULTS

Five of the 6 pregnant cows survived and gave birth to healthy calves. The mean gestation length was 282.8 (S.D. ± 2.2) days and the mean birth weight was 3 1.0 (S.D. ± 6.6) kg.

Animal no. 2 died from urea poisoning during the third series of observations and following administration of 0.35 g/kg urea. The animal showed hyperaesthesia, muscle trembling and slight ataxia after 85 min. Thereafter, clinical signs progressed; the animal showed excessive salivation, frothing from the mouth, laboured respiration, muscular spasms and finally became prostrate. It died 3.0 h after receiving the urea.

The non-pregnant cow, receiving 0.40 g/kg urea, showed initial signs of toxicity 150 min after administration and died 45 min later. The cow receiving 0.45 g/kg had initial signs within 60 min and succumbed 285 min after dosing. Both these cows had progressive clinical signs similar to those observed in animal no. 2.

Blood ammonia-nitrogen levels expressed as the values above initial levels for all animals studied are shown in Figure 1. There was little diurnal variation in the animals receiving no urea, all mean levels recorded being lower than initial values. The maximum mean decline was 1.1 μg/ml of blood at 390 min (mean) after initial sampling. Animals receiving 0.20 and 0.25 g of urea/kg body-weight had mean maximum recorded increases of 3.1 and 3.4 μg/ml of blood 95 and 125 min respectively after dosing and declined gradually to below initial levels at the 6 h sampling. Concentrations in animals receiving 0.30 and 0.35 g urea/kg and showing no clinical signs of toxicity rose to mean maximum levels of 6.1 and 6.0 μg/ml above initial levels tended to plateau for a longer period than in those receiving lower levels, but declined to levels approximating initial levels 6.5 h after dosing. The three animals receiving the fatal doses, 0.35, 0.40 and 0.45 g/kg urea, showed a rapid and continuing increase in blood ammonia-nitrogen concentration. Maximum increases were 27.1, 22.0 and 19.5 μg/ml respectively and were recorded at the final samplings 60, 13 and 15 min before death.

IV. DISCUSSION

The toxic dose of urea is dependent on a number of factors such as diet (Clark, Qyaert and Quin 1951), rate of administration (Dinning *et al.* 1948), and period of starvation (Davis and Roberts 1959). In this experiment one type of ration was given and the animals were dosed at a standard time after feed was available. Under these conditions 0.40 g/kg and 0.45 g/kg proved fatal to the only animals receiving those dose rates while 0.35 g/kg was fatal on one of 12 occasions. Thus, each of the pregnant animals received a dose rate (0.30 or 0.35 g/kg) slightly below the fatal dose on at least three occasions at different stages of pregnancy. All five animals produced viable calves. Although not conclusive because of the small number of animals involved, it would appear that a sudden high intake of urea is unlikely to result in abortion or stillbirths.

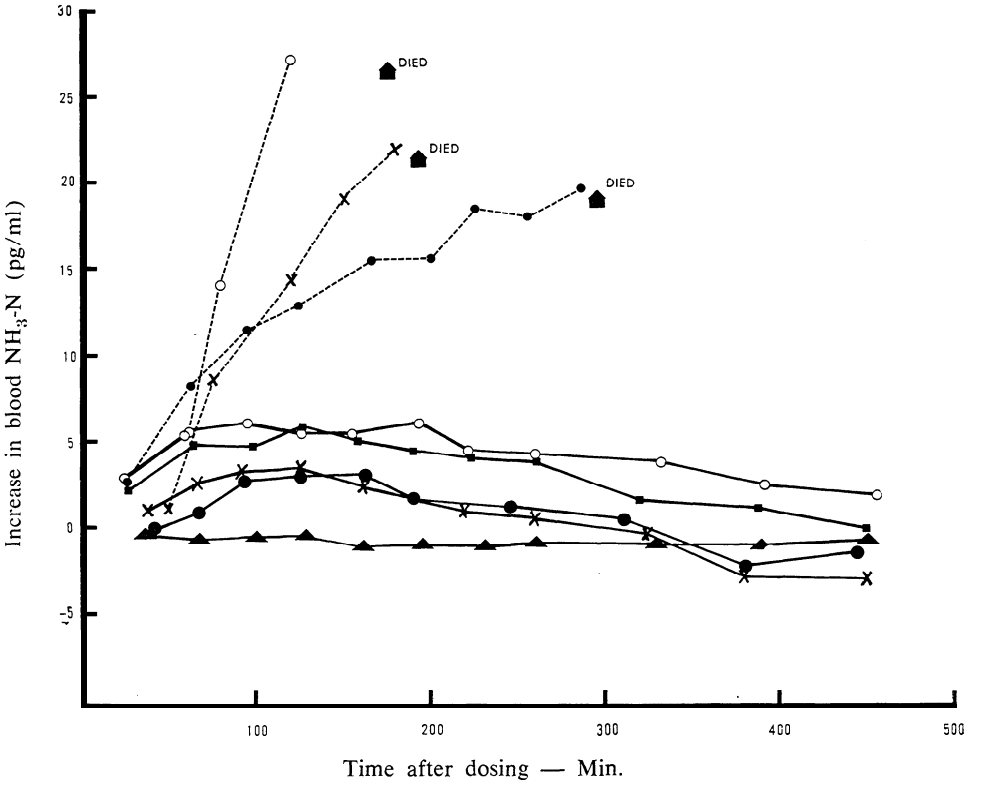

Fig. 1.—Changes in blood ammonia levels in cows following intraruminal administration of urea. ▲—▲ Controls: water only (6 animals); ●—● 0.20 g/kg (2); x—x 0.25 g/kg (2); ○—○ 0.30 g/kg (6); ■—■ 0.35 g/kg (11); ○ – – ○ 0.35 g/kg (1); x – – x 0.40 g/kg (1) and ● – – ● 0.45 g/kg (1).

The effect of lengthy ingestion of high levels of urea by pregnant animals was not studied in this experiment. In this regard, Ryley (1961) recorded two abortions in 10 cows receiving 42.5 g (1.5 oz) urea/head/day but in the same experiment there were no abortions in a similar group given 71 g/head/day. Ryley (unpublished) also gave 227 g (8 oz) urea/head/day to a group of 20 cows, receiving a paspalum hay-sorghum silage ration, for the last 120 days (mean) of pregnancy. The amount of urea in the ration of these cows had been gradually increased from 57 to 227 g (2 to 8 oz)/head/day over a period of 42 days. Nineteen cows produced live calves and one aborted from undetermined causes at 140 days gestation, 88 days after commencement of urea feeding. Since Erb and Holtz (1958) recorded an abortion rate of 5.9% in clinically normal cows, it is probable that this abortion was unrelated to the feeding of urea.

Toxic dose rates of urea recorded in the literature have been recalculated to a g/kg basis, in order to compare our results with those of other workers. Russell, Hale and Hubbert (1962) reviewed different values recorded for the toxic level of single doses of urea and these ranged from 0.40 to 0.88 g/kg in sheep and from 0.27 to 0.32 g/kg in cattle. Their own experiments produced mortality in sheep with doses ranging from 0.28 to 0.72 g/kg. Subsequently

Oltjen *et al.* (1963) reported deaths in sheep after dosing with 0.44 and 0.55 g/kg. These levels can be compared with those of 0.35 to 0.45 g/kg found toxic in our cows. Obviously the toxic dose is variable and as mentioned previously depends on a number of factors.

With the exception of the statement by Davis and Roberts (1959) that no cattle survived in which values for blood ammonia-nitrogen rose above 40 μg/ml, no information could be found on blood ammonia concentrations in cattle following urea administration. In comparisons of our data with those for sheep, published results have been recalculated to the units used in the present paper and values are expressed as increases in blood ammonium-nitrogen above pre-administration- levels. In sheep, the onset of clinical signs were reported at values of 8 to 12 μg/ml (Lewis, Hill and Annison 1957), 6 to 10 μg/ml (McDonald 1958), 2 to 7 μg/ml (Lewis 1960) and 4.9 μg/ml (Oltjen *et al.* 1963). However, Repp *et al.* (1955) recorded levels up to 6.6 μg/ml without clinical signs being apparent. In the present paper clinical signs in three cattle were observed at levels of less than 8, 11 and 19 μg/ml which are slightly higher than the range reported for sheep.

The magnitude of levels that occurred before death in sheep have been reported as 25 to 34 μg/ml in samples taken, presumably, from 30 to 90 min before death (Repp *et al.* 1955), in excess of 28 μg/ml in two sheep just before death (Russell, Hale and Hubbert 1962), and 10.6 μg/ml in sheep about 10 min before death (Oltjen *et al.* 1963). These values are similar to those of 19.5, 22.0 and 27.1 μg/ml taken at 15, 13 and 60 min respectively before death in the present study.

The clinical signs of urea toxicity were similar to those reported by Dinning *et al.* (1948) and Davis and Roberts (1959) in cattle and by Repp et *al.* (1955) in sheep.

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