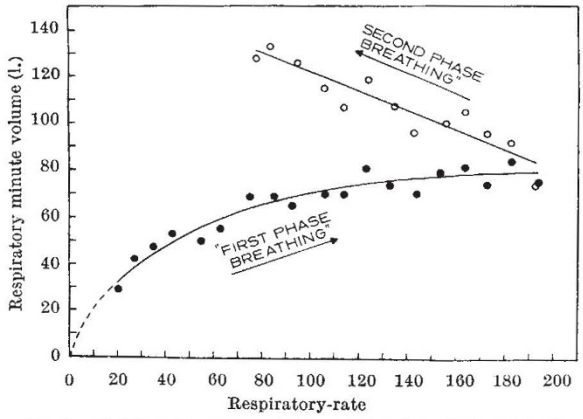

Fig. 2. Relation between respiratory-rate and respiratory minute volume of calves exposed to an atmosphere of 40° C. dry-bulb and 38° C. wet-bulb temperature. (Mean results for 8 animals)

man and Andersen[4] obtained under less stressful environmental conditions in cows, and it confirms their contention that a high respiratory activity is an attempted compensation for a poor heat balance brought about by some other cause.

The inverse relationship between heat tolerance and respiratory minute volume gave rise to the question whether it would be possible to use respiratory-rate (which is easily determined) as an indicator of respiratory minute volume (which is less easily determined). The relationship of these two variables in severely heat-stressed calves is shown in Fig. 2. Owing to the bi-phasic behaviour of respiratory-rate[5,6], in the higher range, a given respiratory-rate is associated with two different values of minute volume: a lower minute volume during the rising phase ('first phase breathing'), and a higher one during the declining phase ('second phase breathing'). Respiratory-rate cannot, therefore, be used to predict respiratory minute volume unless the 'phase' of respiration is known.

W. Bianca

Physiology Department,
Hannah Dairy Research Institute,
Ayr, Scotland.

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Failure of Amino-nucleoside to produce Abnormalities in the Fœtus of the Rat

In an experimental study of urinary tract malformations, an attempt is being made in our laboratory to influence with chemical agents the embryonic development of the kidney. One substance that has been used is the amino-nucleoside derivative of 'Puromycin(R)', which is known to produce increased albuminuria and the nephrotic syndrome in rats. Hallman *et al.*[1] have used this substance in attempts to induce a congenital nephrotic syndrome in experimental animals, and they have described renal tubular dilatation in some offspring of rats treated during the last days of pregnancy.

The test animals used were pregnant albino rats of the Sprague–Dawley strain, weighing 150–200 g. Fifty-one animals were given amino-nucleoside for periods of 7 days, beginning on the fifth to fourteenth day of gestation. Each course of treatment consisted of daily subcutaneous injections of 0·3 ml. per 100 g of body-weight of one of the following solutions of amino-nucleoside in sterile distilled water: 0·375 mg per 100 ml., 0·50 mg per 100 ml., 0·675 mg per 100 ml., and 0·750 mg per 100 ml. (Table 1). Control animals were injected with sterile distilled water. Offspring were killed at intervals up to 2 months after birth and their kidneys were examined histologically. Available sera from offspring were pooled according to litters to make 17 batches, which were examined electrophoretically by the method of Smithies[2]. Parent animals were also killed and examined in a similar fashion.

Table 1. Injection of Pregnant Rats with Amino-nucleoside

Solutions	Day of gestation on which injections were started									
(mg/100 ml.)	5	6	7	8	9	10	11	12	13	14
0·750	1*	1	1	1	1	1	1	0	0	0
	0†	0	0	0	0	0	3	0	0	0
	9‡	11	13	13	12	12	3	0	0	0
0·675	1	1	1	1	1	1	1	1	1	1
	0	6	10	6	7	6	5	6	11	8
	8	0	0	0	0	0	0	0	0	0
0·500	3	3	3	1	1	3	2	1	1	1
	8	6	9	0	0	0	6	0	0	0
	26	21	12	11	11	35	13	13	12	10
0·375	3	1	3	1	1	2	0	3	1	0
	18	10	17	11	13	20	0	25	9	0
	0	0	0	0	0	0	0	0	0	0
Control	3	3	3	3	3	3	3	3	3	3
	32	33	33	27	26	33	33	32	30	34
	0	0	0	0	0	0	0	0	0	0

* No. of mothers.
† No. of offspring examined.
‡ No. of abortion sites.

The highest dosage of amino-nucleoside caused abortion, as determined by the examination of the uterine implantation sites, in most animals. Examination of the 170 living offspring in the experiment disclosed no gross malformations or microscopic abnormalities of the kidneys, and the electrophoretic patterns of serum proteins were normal. No other anomalies were observed. Eight parent animals which were treated with amino-nucleoside solution in a concentration of 0·5 mg per 100 ml. did, however, develop microscopic renal abnormalities consisting of variable tubular dilatation, with proteinaceous precipitates and cast formation. Five of these eight also had electrophoretic patterns of serum protein consistent with the nephrotic syndrome.

These investigations have not produced congenital or developmental abnormalities in the kidneys of rats, and we have not been able to reproduce the findings of Hallman *et al.* That the amino-nucleoside either produced abortion or left the fœtus unaffected, according to the dosage used, suggests that its toxic effect may have been mediated through interference with placental function.

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Jay Bernstein
Ruben Meyer
Donald S. Pickman

Child Research Center,
Detroit, Michigan.

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