Aust. J. Biol. Sci., 1988, **41**, 589–90

Effects of Scopolamine Hydrobromide on the Development of the Chick and Rabbit Embryo

W. G. McBride, P. H. Vardy and J. French

Foundation 41, Developmental Biology Unit, The Women's Hospital, Surry Hills, N.S.W. 2010.

published in *Aust. J. Biol. Sci.*, 1982, **35**, 173–8.

Note on the Paper 'Effects of Scopolamine Hydrobromide on the Development of the Chick and Rabbit Embryo' by W. G. McBride, P. H. Vardy and J. French

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published in *Aust. J. Biol. Sci.*, 1983, **36**, 171–2.

The Journal wishes to bring the following to the attention of readers.

After allegations of fraud were made publicly about the articles cited above, published in the *Australian Journal of Biological Sciences*, a Committee of Inquiry was established by the Board of Foundation 41 to investigate the allegations. The Committee published a report on 2 November 1988 which concludes as follows:

'(a) Deliberate falsification did occur in the paper "Effects of Scopolamine Hydrobromide on the Development of the Chick and Rabbit Embryo" published in the Australian Journal of Biological Sciences, 1982, Vol. 35, pp. 173–8, in that it was falsely stated in that paper—

i. That eight rabbits were the subject of the experiment in New South Wales when only six rabbits were the subject of the experiment in that State.

ii. That the dosages shown under the heading "Oral Ingestion" in Table 2 were correct.

iii. That the foetuses in the experimental group were sectioned.

iv. That eight rabbits contemporaneously obtained from the same suppliers and fed the same diet were used as controls.

'(b) The experiment mentioned in that paper was not conducted in accordance with proper scientific method and was not honestly reported.

'(c) Although criticisms regarding inappropriate controls may be made, we have not determined that deliberate falsification occurred in or in connection with the note published in the Australian Journal of Biological Sciences, 1983, Vol. 36, pp. 171–2.

'(d) The above experiment and its published results does suggest that in relation to the publication of those results Dr. McBride was lacking in scientific integrity.'

The report states that, on 20 September 1982, Ms J. French recorded in a letter to Foundation 41 that her name had, without her knowledge, been used as co-author of the paper which contained statements and data with which she disagreed. On 18 October 1982, seeking employment, Mr P. H. Vardy circulated his C. V. to all members of the Australian Teratology Society, stating that the paper had been written and submitted without the knowledge of either Ms J. French or himself.

The report is signed by the three members of the Committee of Inquiry: the former Chief Justice of the High Court of Australia, Sir Harry Gibbs (chairman); Professor Robert Porter, director of the John Curtin School of Medical Research at the Australian National University; and Professor Roger Short of the Faculty of Medicine, Monash University.

Aust. J. Biol. Sci., 1983, **36**, 171–2

Note on the Paper 'Effects of Scopolamine Hydrobromide on the Development of the Chick and Rabbit Embryo' by W. G. McBride, P. H. Vardy and J. French*

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After the above paper had been published it was discovered that because of difficulty in measuring rabbit water intake accurately with the containers used in the experiment described in that paper the amount of scopolamine hydrobromide ingested by the rabbits was less than as stated. It was therefore decided to repeat the experiment using a different type of water container. The original experiment was carried out in winter and the latter in summer and this could be another factor in the increase in water intake by the does in the present experiment.

Materials and Methods

Ten virgin New Zealand white rabbit does (Tillside Rabbits, Bargo, N.S.W.) weighing between 3·071 and 3·893 kg were mated with a healthy male. Copulation was observed and the day of mating was designated gestation day 1. The mated females were housed individually in polyvinyl-chloride–coated wire cages and were provided with rabbit chow (Doust and Rabbidge, Concord West, N.S.W.) and water *ad libitum*. The water used throughout the experiment was from the Sydney City Water Supply which is known not to contain teratogens.

The does were given scopolamine hydrobromide in the drinking water from the 10th to the 14th day of gestation inclusive. The amount of drinking water, which was prepared daily so that 1 ml contained 10 μg of scopolamine hydrobromide, ingested by each doe was recorded and the mean dose for the 5-day period calculated.

The treated does were killed on the 28th day of gestation and the uteri examined to record the placement of live, dead or resorbed foetuses as well as the number of implantation sites and corpora lutea.

Results and Discussion

Four of the does were found not to be pregnant (Table 1). The foetuses in the experiment were examined for obvious malformations of the skull, body wall and limbs. They were then sectioned to inspect the brain, eye, palate, thoracic and abdominal organs. In all, six pregnant does produced 38 foetuses. The 38 foetuses all exhibited either microphthalmia (34, 89·5%) or buphthalmia (4, 10·5%).

The method of oral administration of scopolamine hydrobromide in the drinking water makes it impossible to measure the exact dose of drug ingested by the doe, as some wastage inevitably occurs owing to movement of the doe in the cage and to the failure of the valve in the drinking tube to cut off the flow of water without some

* *Aust. J. Biol. Sci.*, 1982, **35**, 173–8.

0004-9417/83/020171$02.00

leakage after the doe ceases to drink. If the cages were left empty it was found that approximately 2 ml of water per day leaked from the bottles. However, the maximum possible dosage of scopolamine hydrobromide ingested by the doe is shown in this

Table 1. Effects of scopolamine hydrobromide administered to New Zealand White rabbit does on the 10th to the 14th day of gestation

Controls were as in the original experiment

Doe No.	Weight (kg)	Mean daily dose of scopolamine hydrobromide (μg/kg)	No. of living foetuses	No. with deformities	No. of resorptions
1	3·071	1114	5	5	3
2	3·692	579	10	10	0
3	3·825	444	7	7	0
4	3·893	893	6	6	0
5	3·590	929	0	0	0
6	3·263	658	0	0	0
7	3·460	561	0	0	0
8	3·775	572	6	6	0
9	3·372	914	4	4	0
10	3·222	750	0	0	0

experiment which confirms that massive doses of this drug, when given in the drinking water from the 10th to the 14th day of gestation, will produce malformations, particularly in the eye, in the New Zealand white rabbit foetus.

Manuscript received 27 January 1983, accepted 2 February 1983