DEFORMITIES IN PIGLETS FOLLOWING ADMINISTRATION OF METHALLIBURE DURING SPECIFIC STAGES OF GESTATION

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Paget, Walpole & Richardson (1961) reported that the oral administration of the hydrazine derivative methallibure (1- α -methyl-allyl-6 methylthiobiurea, ICI 33828, Aimax) to rats resulted in a selective and reversible inhibition of pituitary gonadotrophic function. Subsequent work (Gerrits & Johnson, 1964; Polge, 1964) has demonstrated that this compound can be included in the ration and is highly effective for synchronization of oestrus in swine. Satisfactory results have been obtained in many controlled breeding trials and results indicate that methallibure would be of practical use in commercial breeding programmes. Some side effects, such as appetite suppression (Stratman & First, 1965) and inhibition of milk secretion in sows (Gerrits, Johnson & Kraeling, 1965), have been reported but these are not persistent or serious.

One problem with any medicated feed is that quantities in excess of that actually required for feeding during the control period may be purchased and farmers may substitute this for the routine ration of other animals. Call, Barker & Cummings (1969) have reported that the accidental feeding of methallibure to boars would not have any permanent deleterious effect on semen production. Another possibility is that surplus medicated feed might be given to pregnant animals or pregnant females may be inadvertently included in groups fed for routine cycle control. Groves (1967) has reported birth of a normal litter from one gilt accidentally assigned to a 20-day period of methallibure treatment at mid-pregnancy, but there is no other published information on the effects of this drug at other stages of gestation.

A number of pregnant Yorkshire, Hampshire and Lacombe gilts were fed 100 mg methallibure daily for 20-day periods at various stages of pregnancy and the results are summarized in Table 1. Treated gilts were selected from several larger groups which had been inseminated immediately following routine synchronization with methallibure. Animals were artificially inseminated each day they would stand for the 'back-pressure test' in the presence of a boar and most were inseminated on 2 successive days. In all cases, the figures recorded for stage of gestation are calculated from the first day of insemination and may be 1 day longer than the actual gestation.

No deformed or abnormal piglets were observed in the seventy-five litters produced by gilts and sows in the original synchronization trials which did not

receive any additional methallibure during gestation. Similarly, the ten gilts receiving the medicated feed during various intervals after Day 49 also farrowed litters in which all piglets appeared normal. Table 1 shows there was some variation in results obtained when methallibure administration was started between Days 47 and 49. Of the four gilts placed on medicated feed during this short interval, two farrowed litters which contained no grossly abnormal piglets. Gilt No. 9503 had five normal piglets and four others with limb defects. The fourth female, No. 10402, had five mummified foetuses and five live piglets with

TABLE 1
LITTER DATA FROM GILTS FED METHALLIBURE DURING VARIOUS
STAGES OF GESTATION

<i>Gilt</i>	<i>Stage of gestation in days</i>	<i>Litter size</i>	<i>Remarks</i>
20101	80 to 100	18	All piglets normal
20104	79 to 97	11	All piglets normal
19801	76 to 98	7	All piglets normal
5302	72 to 92	5	All piglets normal
503	63 to 83	6	All piglets normal
502	57 to 77	8	All piglets normal
401	54 to 74	10	All piglets normal
8606	51 to 71	11	All piglets normal
8607	50 to 70	11	All piglets normal
8608	50 to 70	6	All piglets normal
7801	49 to 69	10	All piglets normal
10402	49 to 69	10	5 mummified, 5 deformed limbs
1003	48 to 68	4	All piglets normal
9503	47 to 67	9	5 normal, 4 deformed limbs
9601	31 to 51	13	All with cranial and limb defects
5501	30 to 50	11	All with cranial and limb defects
6702	30 to 50	12	All with cranial and limb defects
3404	29 to 49	12	All with cranial and limb defects
6803	29 to 49	6	All with cranial and limb defects
7602	28 to 48	0	Returned after treatment

limb defects. All piglets born to the five gilts receiving methallibure earlier in gestation had obvious skull and limb abnormalities, but individual littermates were affected to varying degrees of severity. The last gilt, No. 7602, did not show oestrus 3 weeks after breeding but did return after the second course of methallibure feeding. It is quite possible this animal was not pregnant during the treatment period.

Most of the affected piglets were born alive, were alert and responded normally to stimuli. All were able to progress by crawling and the less severely affected could stand and walk. On external examination, one obvious visible abnormality was slight to severe flexion of both fore and hind limbs. Deformities of the cranium and mandibles were also apparent in piglets from gilts fed methallibure during the 29- to 50-day period of gestation. Necropsy showed that, in most piglets, the distal segments of the limbs were in fixed flexion because of contracted tendons. The principal long bones were slightly shorter and thicker than normal. Heads were disproportionately short, the mandible was distorted and the bones of the dorsal and dorso-lateral sides of the cranium were deformed. The scalp showed complete or partial alopecia correlated with

PLATE 1

Severely deformed piglet farrowed by a gilt that was fed methallibure from Day 29 to 49 of gestation. Abnormalities of the cranium and flexion of both fore and hind limbs are readily apparent.

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the degree of abnormality in the underlying bones. Plate 1 illustrates the gross appearance of one of the most severely affected animals. These lesions are similar to those induced in rat fetuses by another hydrazine derivative, 1-methyl-2-para (isopropylcarbamoyl) benzylhydrazine, when injected into pregnant rats on Day 11 or 12 of gestation (Chaube & Murphy, 1964).

This trial demonstrates that methallibure appears to be a potent teratogenic agent in pigs when fed for 20-day intervals during the first 49 days of gestation.

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