Use of Chorionic Gonadotropin to prevent Early Embryonic Mortality in Temporarily Fasted Mice

When studying the pathogenesis of the infertility in female mice caused by depriving them of all food for short periods during early gestation[1], it was found that the immediate cause was either failure of implantation or death of the embryo after implantation. In the latter case, it appeared from the histopathology that the primary lesion occurred in the deciduoma. This was followed by the death of the embryo, possibly due to interference with its nutrition.

The minimal starvation required was the 48-hr. period from the fourth to sixth day after œstrus or third to fifth day after the formation of the copulation plug. Such fasting rendered all matings infertile. However, when injections of 5 I.U. of chorionic gonadotropin were given once daily to each of ten mice during the period when they were being starved, the embryos of all mice survived until at least the third day after the end of the fast. When examined at this time none of the twelve control mice, fasted but not injected, was pregnant. It was assumed from the results of earlier work that embryos had developed but had died and been reabsorbed. When chorionic gonadotropin was given to 16 mice in a third group, over the period from the start of starvation until five days after its end, the embryos of ten appeared normal on the sixth day after the end of fasting. The embryos of three were starting to degenerate and three mice were not pregnant. Progesterone in daily doses of 0·5 mgm. had a similar protective effect.

This suggests that the pathogenesis of the embryonic mortality involves the anterior pituitary–ovarian endocrine system.

T. J. McClure

Ruakura Animal Research Station,
Hamilton,
Department of Agriculture,
New Zealand.

[1] McClure, T. J., *Nature*, **181**, 1132 (1958); *J. Physiol.*, **147**, 221 (1959).

Oxygen Consumption by Tissues from Rats injected with L- or D-Thyroxine

It has been shown by a number of investigators that L-thyroxine is more active *in vivo* than is D-thyroxine[1]. In most *in vitro* systems, however, the D- and L-isomers are equally effective. The equal activity of D- and L-thyroxine in altering the morphology of mitochondria and in 'uncoupling' oxidative phosphorylation are examples of this[2,3]. Previous experiments[4] in this laboratory have compared the distribution and excretion of labelled D- and L-thyroxine labelled with iodine-131 following a single injection of a tracer quantity of each compound into the tail vein of the rat. Initially, D-thyroxine was concentrated to a greater extent in the liver and kidney than was L-thyroxine, but after 24 hr. the concentrations were approximately equal. However, the concentration of D-thyroxine in tissues such as muscle, brain and skin was much less than the concentration of L-thyroxine. This difference in distribution to the peripheral tissues was of such magnitude as to suggest a possible basis for the different activities of the two isomers *in vivo*. Others have shown[5,6] that the oxygen consumption of certain tissues (for example, liver, kidney and muscle) from animals injected with DL-thyroxine is significantly greater than normal, whereas that of other tissues (for example, brain) is not increased. The current investigation was undertaken to determine whether the differences demonstrated in the distribution of the two isomers could be correlated with a difference in their ability to stimulate the oxygen consumption of the several tissues.

Adult male Wistar rats, 4–6 weeks post-thyroidectomy, were used in this experiment. The treated animals were injected subcutaneously for 4 days with either D- or L-thyroxine (6 mgm./kgm.). (D-thyroxine was provided through the kindness of Dr. L. G. Ginger, of Travenol Laboratories, Inc., Morton Grove, Illinois. L-thyroxine was furnished through the kindness of Dr. A. E. Heming, of Smith, Kline and French Laboratories, Philadelphia, Pa.) The sodium salt of each isomer was dissolved in 0·02 *N* sodium hydroxide and 0·9 per cent sodium chloride. All animals were fasted 24 hr. before being anæsthetized with ether and exsanguinated. The various tissues were rapidly excised and placed in ice-cold Krebs–Ringer–phosphate solution. All tissues were prepared in duplicate. Liver, kidney and heart slices prepared by the Deutsch technique[7] were made smaller by cutting with scissors. Each diaphragm was cleared of fat and connective tissue, and its central portion was removed; the hemi-diaphragms then were placed in separate flasks. Specimens of brain were prepared by removing the larger tracts of white matter and forcing the remaining tissue through a syringe and No. 18 needle. After weighing, the tissues were placed in chilled Warburg flasks containing the incubation medium (Krebs–Ringer solution buffered with 0·01 *M* sodium phosphate with 100 mgm. per cent glucose). The flasks were gassed with 100 per cent oxygen for 5 min.; oxygen consumption was determined at 37° C.

It may be noted in Table 1 that with slices of liver from animals injected with either D- or L-thyroxine the oxygen consumption is almost identical; in both cases the Qo_2 is significantly greater than that of the control. The same result was also obtained with kidney slices. With heart and diaphragm, on the other hand, there is a significant difference between the animals injected with L-thyroxine and those injected with D-thyroxine; in both tissues the Qo_2

Table 1. Oxygen Consumption by Various Tissues from Rats injected with L- or D-Thyroxine

	Control Qo_2 (10 rats)	L-Thyroxine Qo_2 (10 rats)	D-Thyroxine Qo_2 (10 rats)	*P* Control vs. L-thyroxine	*P* Control vs. D-thyroxine	*P* L-Thyroxine vs. D-thyroxine
Liver	1·40 ± 0·06*	1·94 ± 0·03	1·91 ± 0·07	< 0·001	< 0·001	> 0·1
Kidney	3·03 ± 0·13	3·79 ± 0·19	3·84 ± 0·11	< 0·01	< 0·001	> 0·01
Heart	1·21 ± 0·06	1·51 ± 0·08	1·30 ± 0·04	< 0·01	< 0·001	< 0·001
Diaphragm	1·11 ± 0·03	1·48 ± 0·04	1·29 ± 0·04	< 0·001	< 0·001	< 0·01
Brain	1·66 ± 0·04	1·51 ± 0·04	1·60 ± 0·04	< 0·01	> 0·1	> 0·1

* Standard error of the mean, Qo_2 = cu.mm. of oxygen per mgm. wet weight per hr.