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Roberto Colombo

Placental metabolism of ^{14}C-lactate, intrauterine position and number of implantations in the rat

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SEZIONE III
(Botanica, zoologia, fisiologia e patologia)

Zoologia. — *Placental metabolism of* ^{14}C-*lactate, intrauterine position and number of implantations in the rat* (*). Nota di ROBERTO COLOMBO, presentata (**) dal Socio S. RANZI.

RIASSUNTO. — Sulla base di precedenti esperienze, si è voluto determinare l'affinità per il ^{14}C–lattato delle placente di ratto, al 15° giorno di gestazione, relativa alla loro diversa posizione intrauterina. Una differente affinità per questo substrato è stata notata solo quando il numero degli impianti era maggiore di 6 per ogni corno uterino. Sulla base di questi dati e di quelli precedentemente trovati è stato possibile dare una spiegazione di questo fenomeno.

In animals presenting the gestative phenomenon, the maternal uterus represents the embryo's life environment which, through its physical, chemical, and chemico-physical parameters, may affect the development of the embryo itself.

It is well known that the bipartite uterus of the Rodent shows different degrees of blood supply along its length (Barr M. and Brent R. L., 1970; Colombo R. and Giavini E., 1972; McLaren A. and Michie D. 1960; Woollam D. H. M. and Millen J. W., 1962), producing a different metabolism in embryos from the same mother, probably due to a different oxygen supply. Embryos implanted in paraovarian positions of the uterus (implantation seats corresponding to the tubal end of the uterine horn) which are generally considered ischemic show a lower mitochondrial dehydrogenase activity than the siblings implanted in the paravaginal position of the uterus (implantation seats corresponding to the vaginal end of the uterine horn) (Colombo R. and Giavini E., 1975); furthermore, after inhibition of LDH by means of K-oxamate, they show a higher pyruvate accumulation than embryos implanted in districts with a greater blood supply (Colombo R. and Giavini E., 1973); at the same time, spontaneous foetal reabsorption is much more frequent in paraovarian uterine districts (Colombo R. unpublished data) which evidently present suboptimal development conditions.

Moreover, it was decided to test the metabolic power of the placentae of paraovarian and paravaginal embryos with respect to ^{14}C-lactate. In fact, as the embryos in paraovarian areas of the uterus are in hypoxic conditions,

(*) Lavoro eseguito nell'Istituto di Zoologia dell'Università statale di Milano con contributo del C.N.R. (76.01480.04).

(**) Nella seduta del 10 dicembre 1977.

they consequently have a higher production of lactate (Colombo R., Duzioni A. and Landoni C., 1977 in press) than siblings implanted in paravaginal areas.

Usually the foetal lactate is transferred to the placenta, which at least partially metabolizes it (Friedmann E. A. and Coll., 1960).

Accordingly, the placentae of paraovarian embryos having a greater availability of lactate should present a more active enzymatic pool and consequently a more outstanding ability in metabolizing lactate than the placentae of paravaginal embryos.

From 30 pregnant females of white rat (Sprague Dawley stock) at the 15th day of gestation, the placentae nearest to the tubal and the vaginal ends were drawn from each uterine horn; these placentae were weighed, finely sliced with a blade and then incubated for one hour in a solution, the composition of which, expressed in micromoles, was the following: K^+ 50, Na^+ 80, Mg^{++} 10, Phosphate 40 and Cl^- 100 (Villee C. A. 1953).

^{14}C-lactate, 5 μCi, was added to the incubation medium.

At the end of the incubation period the pyruvate produced was precipitated as 2,4 phenylhydrazone; the precipitate was collected and washed several times by vacuum filtration through a HAWP HA 0,45 μ, 2,5 mm diameter millipore filter.

After drying, filters were suitably prepared and radioactivity was tested by liquid scintillation using the Packard Mod. 3320 spectrometer.

Results

The results are given in the following Tables.

Table I synthetizes the results obtained with respect to the females showing more than 6 implantation seats in each uterine horn; Table II synthetizes results regarding females presenting, inversely, less than 6 implantation seats for each uterine horn; Table III compares the metabolic capacities of high (paraovarian) placentae taken from uterine horns with more than and fewer than 6 implantation seats.

Discussion

As can be clearly seen, the working hypothesis has been fully verified.

A new and very interesting fact has however emerged. When in a single uterine horn the number of embryos is lower than a particular standard value, no difference can be ascertained in the metabolic capacities of the placentae taken from the various uterine areas considered; on the contrary, as far as the pyruvate from ^{14}C-lactate production is concerned, this tends to balance on definitely low levels in both types of placentae (Table II).

In our opinion, this fact would mean that when in a single uterine horn the implantation number lies within the range of a certain standard value (six in this case), embryos preferably occupy those uterine zones offering the best periembryonic environmental conditions. These areas, owing to their rich blood supply and the low number of implantations, allow the embryos to develop a not strictly anaerobic metabolism (Colombo R. and Giavini E., 1975) and consequently a relatively scarce production of lactate.

TABLE I

Data referring to placentae from females with more than 6 implantation seats for a single uterine horn.

(Mean ± M.S.E. with *n* in parentheses).

Uterine zone	Average weight of placentae	nmoles Pyruvate/tiss.gr./h
High (true paraovarian) . . .	0,265 ± 0,009 g (18)	1,027 ± 0,084 (18) (*)
Low (paravaginal)	0,307 ± 0,008 g (19)	0,654 ± 0,064 (19) (*)

(*) Data with significant difference ($p < 0{,}05$).

TABLE II

Data referring to placentae from females with fewer than 6 implantation seats for a single uterine horn.

(Mean ± M.S.E. with *n* in parentheses).

Uterine zone	Average weight of placentae	nmoles Pyruvate/tiss.gr./h
High (false paraovarian). . .	0,315 ± 0,006 g (13)	0,157 ± 0,006 (13)
Low (paravaginal)	0,305 ± 0,001 g (15)	0,189 ± 0,007 (15)

TABLE III

Data referring to placentae from females with more than and fewer than 6 implantation seats for a single uterine horn.

(Mean ± M.S.E. with *n* in parentheses).

Uterine zone	Average weight of placentae	nmoles Pyruvate/tiss.gr./h.
High (true paraovarian) . . .	0,265 ± 0,009 g (18)	1,027 ± 0,084 (18) (*)
High (false paraovarian). . .	0,315 ± 0,006 g (13)	0,157 ± 0,006 (13) (*)

(*) Data with highly significant difference ($p < 0{,}01$).

Practically, placentae nearest to the ovary are not, in this case, actual paraovarian placentae, inasmuch embryos, owing to their comparatively low number, may neglect this uterine area, implanting themselves in those zones offering better development conditions.

It follows from the above considerations that placentae relevant to these embryos receive but little embryonal lactate and are consequently scarcely able to metabolize this substrate.

Inversely, when the number of implantations per single uterine horn overruns the standard value, embryos occupy all free uterine positions, even those presenting sub-optimal periembryonic environmental conditions.

Thus two classes of embryos are formed: those implanted in ischemic paraovarian districts, with a strictly anaerobic metabolism and those implanted in middle and paravaginal districts, presenting a trend to oxydative metabolism.

The preceding data agree with present knowledge on the development of the embryonic mitochondrial system.

The majority of mitochondrial enzymes, like the pyruvic dehydrogenase complex strongly increase their activity during the late gestation period (Knowles S. E. and Ballard F. J., 1974). But also for this mitochondrial enzyme, as has been demonstrated for succinic dehydrogenase (Colombo R. and Giavini E., 1975), there could exist a differential development depending on the periembryonic environmental conditions of the uterine area of implantation.

On the basis of the data obtained it might appear that for embryos of the lower uterine areas the pyruvic dehydrogenase complex would develop earlier than in paraovarian embryos; thus, a part of the pyruvate produced by embryos implanted in a paravaginal position is converted into Acetyl-CoA and utilized within the Krebs cycle.

This fact may suggest an explanation for the lower production of lactate by the paravaginal embryos (Colombo R., Duzioni A. and Landoni C., 1977 in press) and the scarce ability of their placentae to convert lactate into pyruvate.

At the same time, paraovarian embryos produce a great amount of lactate and their placentae, having normally great amounts of embryonic lactate to metabolize, develop a particular affinity for this substrate, as can easily be verified from experimental data.

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