Pathways of Carbohydrate in the Bovine Endometrial-Chorionic Unit as an Embryonic Nutrient

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Low fertility of cattle has long been an important source of economic loss to breeders and dairy-farmers.

Based upon the studies of reproductive performance carried out using a total of 1987 records of 881 cows, covering a period of 24 years, from Holstein herds of National Institute of Animal Industry, it was estimated that maximum rate of recurrence was 60 days in post-partum breeding interval, 100 days in postpartum conception, 375 days in calving interval, and that about 20.5% of cows required three or more services per conception and 34.3% showed an early embryonic mortality[1].

Most of these low fertilities of cows seem to be not caused by some gross abnormal features in the genitalia, whereas little is known regarding what could be attributable to variations in the pregnancy preparation of the internal genitalia for conceptus.

It is well known[2),3)] that a major energy source at embryonic stage is sugars, and sugars play a central role in the biosynthetic activity of blastocyst. On the other hand, no reducing sugar has been detected in the bovine uterine milk (uterine fluid during pregnancy)[4].

The present paper summarizes information obtained by a series of research of "studies on the uterine secretion of cow"[5)~11)] in relation to the sugar provision for embryonic nutrition.

Detection of sugar and polyol constituents[5)]

Presence of glucose, fructose, sorbitol and inositol was confirmed in the uterine fluid taken from healthy cows during estrous cycle and at 20–40 days of pregnancy by means of gas-liquid and thin-layer chromatographies.

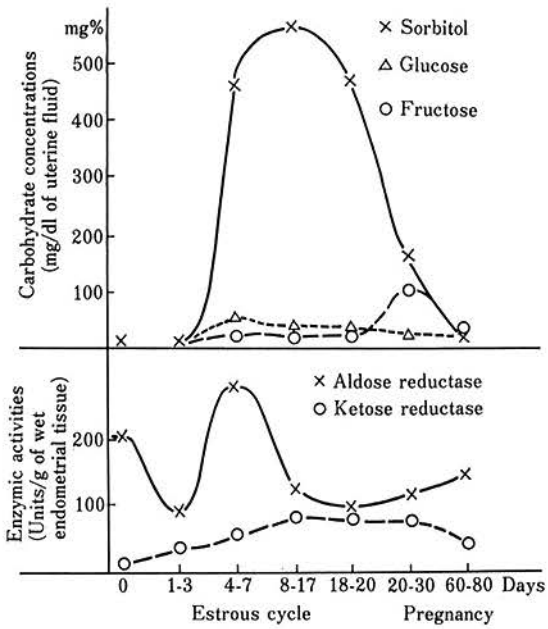


Fig. 1 Carbohydrate concentrations in uterine fluid and enzymic activities in endometrium of the cow during estrous cycle and pregnancy. N=5

Levels of sugar and polyol contents[6),7)]

Concentrations of fructose, glucose and sorbitol in the uterine fluid were determined at various stages of estrous cycle and during 20–80 days of pregnancy by the method of gas-liquid chromatography. Concentrations of these sugars are shown in Fig. 1.

A major component of carbohydrate in the uterine fluid was sorbitol, which showed a peak amount in mid-luteal stage. The highest rate of increase of sorbitol occurred at an early luteal stage (estimated days 4–7 after ovulation). The high level of sorbitol was maintained until the onset of the next estrus, or when the animal came into conception, it vanished within the first month of pregnancy.

Component of carbohydrate in maternal blood, uterine fluid and foetal fluids[6),7),8)]

Distribution and concentration of glucose, fructose and sorbitol in maternal blood, endometrial tissue, uterine fluid, chorion, allantoic fluid and foetal blood were shown in Fig. 2.

The carbohydrate constituents in these materials differ definitely with different materials, namely, a major component was glucose in maternal blood and endometrial tissue, sorbitol in uterine fluid and chorion, and fluctose in allantoic fluid and foetal blood.

Site of sorbitol production[6),7),9)]

The ability of genital-organ tissue to produce sorbitol has been shown to coincide with the distribution of sorbitol. The oviduct and cervical mucosa in which no sorbitol was

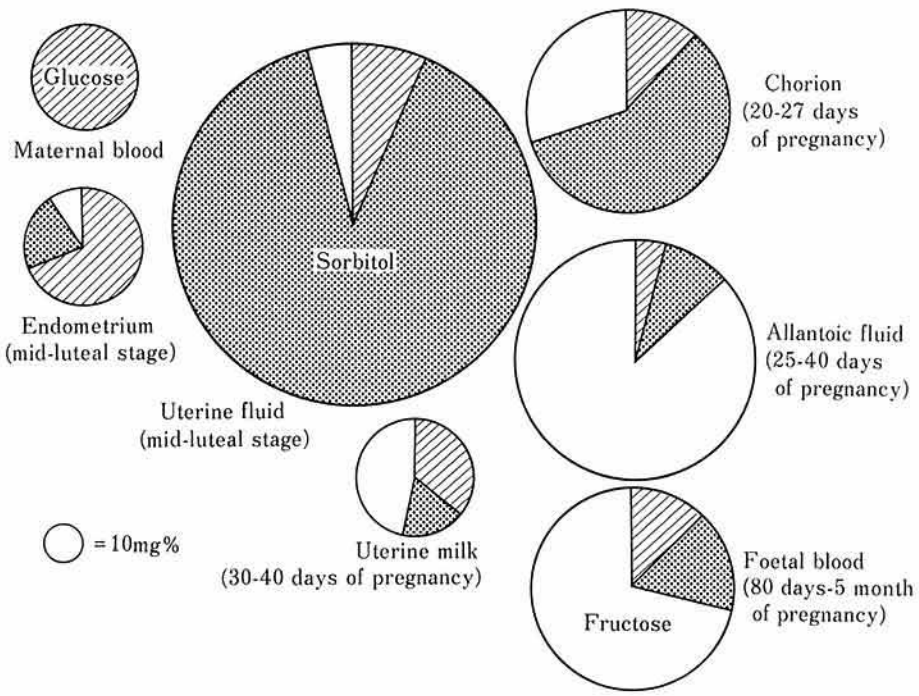


Fig. 2 Components of carbohydrate in maternal blood, uterus and foetus of the cattle

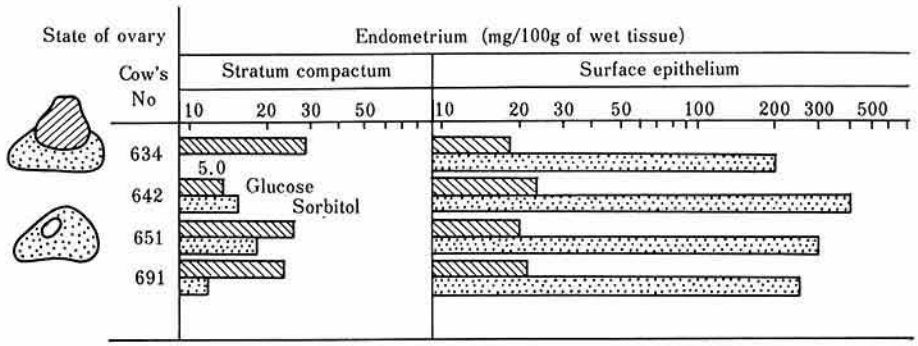


Fig. 3 Distribution of glucose and sorbitol in endometrium of the cow at mid-luteal stage of estrous cycle

found were lacking of the ability to produce sorbitol. Sorbitol was present exclusively in the surface epithelial layer (Fig. 3), and it disappeared in coincidence with the destruction of the surface epithelium during early stage of pregnancy.

The convertion of glucose to sorbitol was confirmed by incubating the homoginated fluid from the surface epithelial cells with glucose and NADPH.

These data indicates that sorbitol is produced in the surface epithelial cells of endometrium of the cow.

Period of sorbitol production[6),8)]

The time of sorbitol production has been shown to coincide with the time when the rate of increase of sorbitol concentration was increasing rapidly and the activity of aldose reductase in uterine fluid and endometrium.

The highest increasing rate of sorbitol was found to coincide with the peak of aldose reductase activity at early luteal stage, while a little or non-detectable sorbitol occurred at the stages of estrus, mid-luteal during estrous cycle and pregnancy (Fig. 1).

Fate of sorbitol in bovine foetal chorion[7),8),9)]

Hers (1960)[12),13)] reported that with sheep the occurrence of fructose in the foetus took place by a two-step reaction involving the reduction of glucose to sorbitol (in the placenta), and oxidation of sorbitol to fructose (in the foetal liver). However no information on the pathway of the carbohydrate change during preplacental period was given.

The activity of ketose reductase: E.C.1.1.1.14 (for fructose formation) was detected by means of histochemical examination. Distinctly positive result was obtained with the trophoblastic cells of the chorion on 20, 25, 30th day of pregnancy.

The conversion of sorbitol to fructose was confirmed by gas chromatography, during the incubation of mixture of enzymic preparation from the bovine chorion, sorbitol and NAD.

These observations on the distribution of ketose reductase, the ability of chorion to produce fructose, decrease of sorbitol level in the uterine fluid after pregnancy (see Fig. 1) and high level of fructose in foetal fluids suggest that sorbitol provided by the endometrial surface epithelial cells was converted to fructose in the chorion within the first month of pregnancy.

The activity of aldose reductase: E.C.1.1.1.21 (for sorbitol formation) was detected in the chorion, too. Aldose reductase activity was increased with the advance of pregnancy (Fig. 4). This seems to indicate that chorion does not assume the ability to produce sorbitol until after a month of pregnancy.

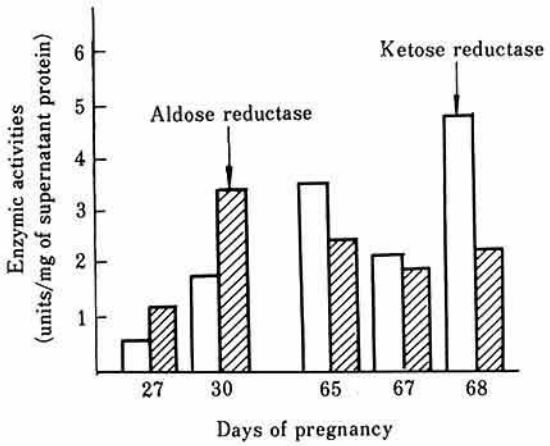


Fig. 4 Activities of aldose reductase and ketose reductase in the bovine foetal chorion.

Stimulation of sorbitol production by ovarian hormones[10]

Effects of ovarian hormones on the sorbitol production were detected by means of injection of estradiol and progesterone into the uterine stroma of ovariectomyzed cows. Estradiol injection alone did not stimulate the sorbitol production. On the contrary, progesterone showed a stimulating effect which was further enhanced in collaboration with estrogen. Increasing dose of progesterone to estradiol appeared to enhance the synergistic actions of the two hormones.

Route of biosynthesis of foetal fructose

The above facts suggest that there are three different ways by which fructose is produced with the advance of pregnancy, as summarized as follows.

1) Within the first month of pregnancy, glucose is converted to sorbitol in the endometrial surface epithelium, and sorbitol is oxidized to fructose in the chorion.

2) After a month of pregnancy, the chorion is the site of sorbitol and fructose formation, and foetal liver is also able to form fructose.

3) After placentation, sorbitol is formed in the foetal placenta, and changes to fructose in the foetal placenta and the foetal liver.

Sorbitol production in the uterus of sterile cows[9),11)]

Carbohydrate components and aldose reductase activity were determined quantitatively in the uterine fluid and the endometrial tissue of sterile cows, and were compared with those in normal cows.

Sorbitol, which is the main carbohydrate component of uterine fluid in normal cows was almost absent in the four sterile groups: a) both large follicle and functional corpus luteum present in the ovary, b) cystic follicle present in the ovary without corpus luteum, c) ovarian atrophy, and d) hydrometra and myxometra at mid-luteal stage (Figs. 5, 6). However, no appreciable difference in the aldose reductase activity was recognized between the sterile and the normal groups.

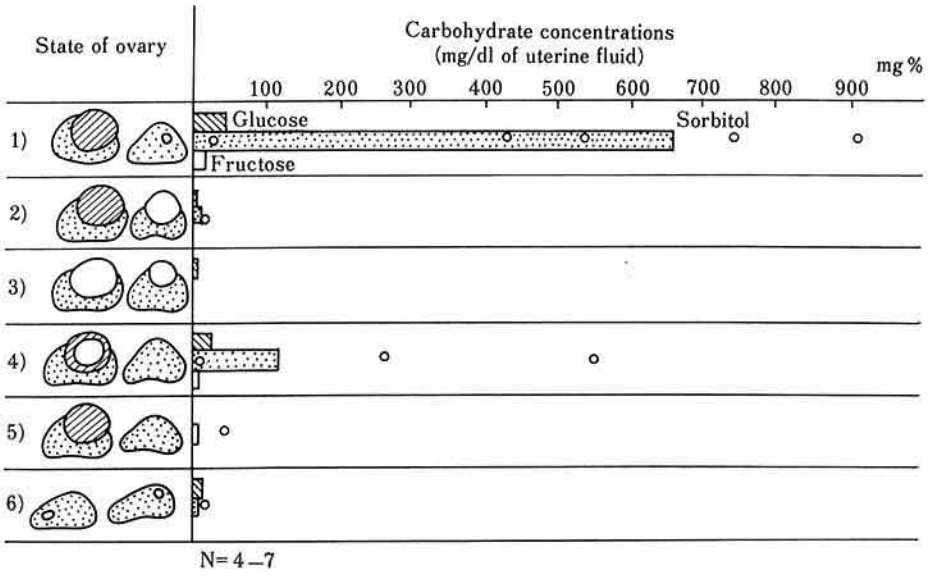
A remarkable difference observed with the sterile groups is that the concentration of glucose (substrate of sorbitol) in the endometrial surface epithelial layer was significantly lower than that in normal group (Fig. 6).

Under incubation with the enzymic preparation from endometrium of sterile cows, addition of glucose into the medium stimulated the production of sorbitol.

These findings indicate that the poor sorbitol formation may conceivably be attributable to the failure of the glucose, in the maternal blood, to penetrate to the site of aldose reductase in the endometrial surface epithelial cells in the sterile cow.

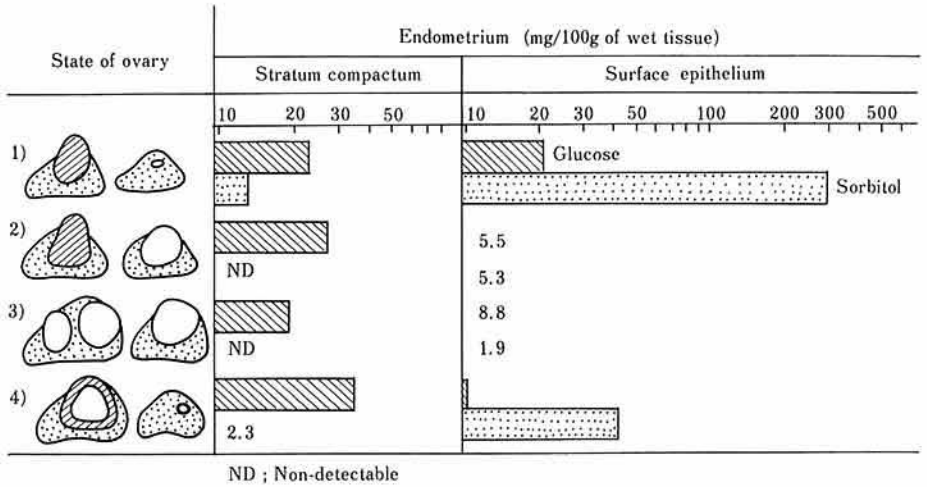
In the cystic corpus luteum group, sorbitol concentration in the uterine fluid and the endometrial tissue varied from nil to near normal.

Sorbitol formation in the endometrial tissue showed a close relationship with the appearance of high pseudostratified columnar type of endometrial epithelial cellular layer and existence of functional corpus luteum



State of ovary:
1) Normal (mid-luteal stage) 2) Both large follicle and functional corpus luteum present 3) Follicular cyst 4) cystic corpus luteum 5) Hydrometra and myxometra (mid-luteal stage) 6) Ovarian atrophy

Fig. 5 Concentrations of carbohydrates in uterine fluid of sterile cows



ND ; Non-detectable

Fig. 6 Concentrations of glucose and sorbitol in the endometrial tissue of sterile cows

in the ovary without large or cystic follicle.

Conclusion

Sorbitol was major component of carbohydrate in the uterine fluid of the cow, and was converted to fructose in the foetal chorion.

The endometrial surface epithelium was the site of sorbitol formation.

Poor sorbitol formation was found in certain sterile cows.

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