Effects of Various Degrees of Undernutrition of Mice on Pregnancy and Conceptus

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Summary. Maternal intake of drastically ($^1/_2$ of control) and substantially ($^1/_3$ of control) reduced feeding was studied in pregnant mice during gestation and embryonic development. Resorptions, fetal mortality rate and fetal weight were significantly affected by maternal undernutrition during the treatment period. The number of fetuses with intrauterine weight retardation was also significant.

Various nutritional factors are known to affect the normal course of pregnancy and embryonic development of different species of animals[1]. Drastically reduced nutritional intake has been shown to have adverse effects on conception[2], implantation of the fertilized ova[3], endocrine functions of the ovary, weight of the mother and the conceptus[4], as well as the intrauterine development and survival of the embryo[5,6]. Severe protein deficiency during gestation in rats was found to reduce birth weight and growth of the offspring[7]. Nutritional deprivation during pregnancy was shown to produce excess fetal mortality and intrauterine growth retardation in monkeys[8], as well as in humans[9].

This report presents data on the effects of various degrees of nutritional intake of mice on the maintenance of pregnancy, and intrauterine growth and survival of the fetus.

Materials and methods. Randomly bred albino female mice (Wistar derived-strain), 85 days old, were mated with males of the same strain. The day of mating, confirmed by either sperm in vaginal smears or a vaginal plug, was considered day 0 of pregnancy. The diet consisted of standard laboratory chow (in pellet form), with the following guaranteed analysis from the manufacturer: protein 23%, fat 4.5%, fiber 6%, ash 9%, NFE (Nitrogen Free Extract – by difference) 47.5% and moisture content 10.0%. Control mice received 5 g of food daily throughout pregnancy. The substantially underfed mice received 3.5 g of food daily and the drastically underfed mice received 2.5 g. Thus, their daily food intake was $^2/_3$ and $^1/_2$, respectively, of the controls. Fresh water was available ad libitum to all mice. All mice were weighed daily and killed on day 18 of pregnancy. Their uterine horns were opened and examined for implantations, early and late resorptions. The fetuses were removed, weighed and examined for external malformations. The data were analyzed for statistical significance by the Student *t*-test[10].

Results. There was evidence that both drastic and substantial underfeeding of female mice adversely affect

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Addendum. Feed analysis[a]

Protein (%)			23.0
Fat (%)			4.5
Fiber (%)			6.0
NFE (Nitrogen free extract by difference, %)			47.5
Energy (KCal/g)			4.25
Moisture content (%)			10.0
Ash (%)			9.0
		Vitamins	
Calcium (%)	1.20	Carotene (ppm)	6.5
Phosphorus (%)	0.86	Thiamin (ppm)	17.7
Potassium (%)	1.10	Riboflavin (ppm)	8.0
Magnesium (%)	0.21	Niacin (ppm)	95.0
Sodium (%)	0.48	Pantothenic acid (ppm)	24.0
Chlorine (%)	0.58	Choline (ppm × 100)	22.5
Fluorine (ppm)	35.0	Folic Acid (ppm)	5.9
Iron (ppm)	198.0	Pyridoxine (ppm)	6.0
Zinc (ppm)	58.0	Biotin (ppm)	0.07
Manganese (ppm)	51.0	Vitamin A (IU/g)	15.0
Copper (ppm)	18.0	α-Tocopherol (IU/lb)	29.8
Cobalt (ppm)	0.4	Ascorbic acid (mg/g)	–
Iodine (ppm)	1.7		

[a] Nutrients expressed as percent of ration except where otherwise indicated.

Effects of various degrees of underfeeding of mice on pregnancy, fetal weight and survival

Average food intake per day	5 g (control)	3/5 g ($^2/_3$ of control)	2/5 g ($^1/_2$ of control)
No. of mice mated	10	10	10
Pregnant %	90	40[a]	20[a]
Died %	0	0	20[a]
Maternal body weight gain (+) or loss (–) during pregnancy (%)	+34	–20[b]	–30[b]
No. of fetuses born	115	11[a]	2[b]
Av. No. of living fetuses extracted by cesarian section/pregnancy[c]	12.8	0	0
Dead fetuses; *resorbed* + *dead* × 100 total implants (%)	7.4	100[b]	100[b]
Av. fetal weight (g)	1.3	0.7[b]	0

[a] Significant from control at $p = 0.05$.
[b] Significant from control at $p = 0.01$.
[c] Dead fetuses were defined as those which were fully developed and approached normal size expected for that particular day. The fetus was considered life if there was an active flow of blood from the umbilical cord and/or pinching the skin with fine forceps produced a noticeable contraction.

conception, the normal course of pregnancy, and the intrauterine development and viability of the conceptus. (Table and Addendum.)

The degree of severity of these effects was influenced by the amount of daily food provided during pregnancy. Prenatal values for live fetuses, dead fetuses and resorption sites and fetal weights were significantly affected by maternal underfeeding. Pregnancy rate was also adversely affected by the reduced nutritional intake.

Discussion and conclusion. Drastic nutritional deprivation resulting in interruption of pregnancy or loss of the conceptus has been well established. However, effects of less severe undernutrition has not received sufficient attention. The above experiment demonstrated that with drastic ($^1/_2$ of control diet) underfeeding only 20% of the mated mice conceived. With lesser but still substantial ($^2/_3$ of control diet) undernutrition the conception rate of mated mice was 40%. The same dietary restrictions when practiced throughout pregnancy had severe effects on the intrauterine survival of the embryos. Further perinatal and postnatal studies are needed since reduced dietary intake during pregnancy is gaining popularity.

Central Venous Pressure: Normal Value and Length of Body

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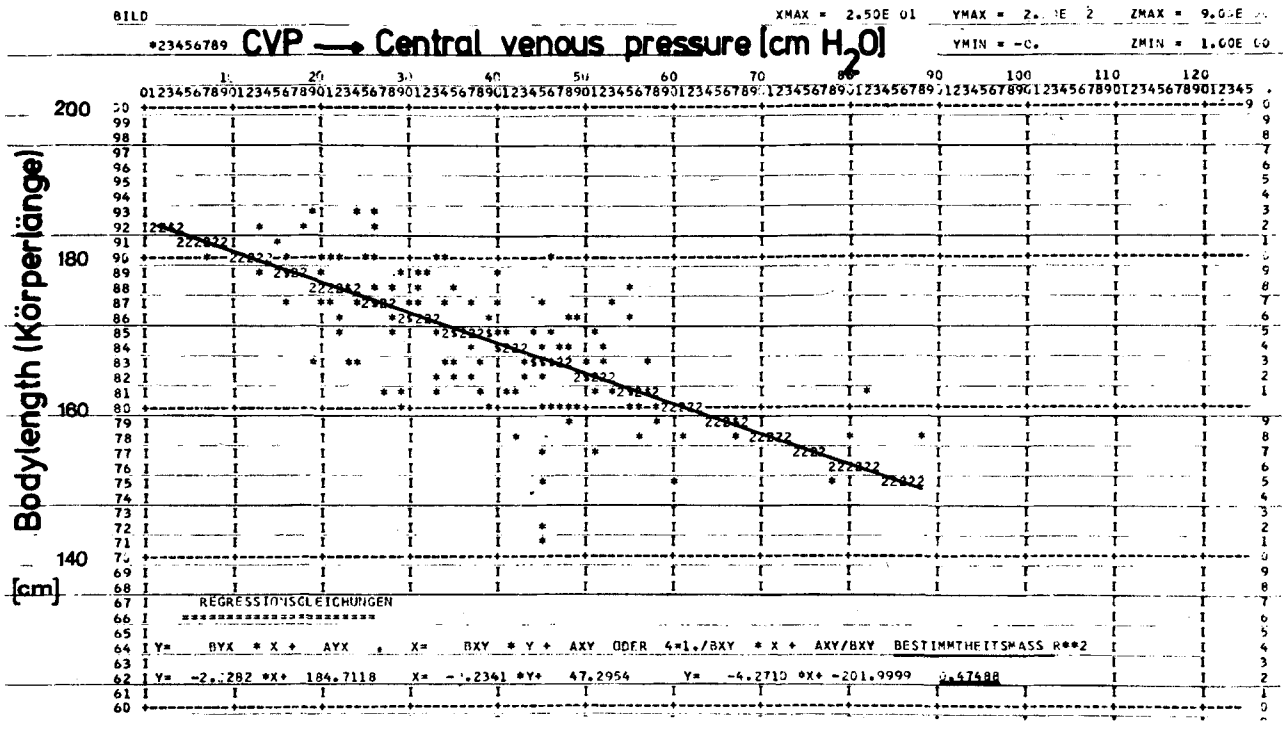
Summary. The CVP ranges between 2 and 12 cm H_2O, and has an 'error' of 2 l of blood. In 172 normal persons, we found a correlation between the CVP and the length of the body.

The clinical meaning of the central venous pressure is not finally determined because of the wide physiological norm. The deviation range is stated to be 2–12 cm H_2O and has, corresponding to the elasticity coefficience E'[1], an 'error' of approximately 2 l of blood. There is no doubt that a constant relation is present between the intrathoracic blood volume and the central venous pressure at rest; but this does not apply to shock, exsiccosis or renal insufficiency[2].

Changes of venous tonus, respiration, heart frequency and cardiac output play a crucial role here. To determine exact physiological limits of normal, we have measured the central venous pressure at rest in 172 people with a healthy blood circulation between the ages of 3 and 73 years, after the method of GAUER and SIECKER[1]. The simultaneous registration of the ECG made the exact evaluation after the P-wave possible. As according to KNEBEL and WICK[3] the expiratory phase of respiration



The correlation between the body length and central venous pressure (n = 172) gives the following regression equation:

$$Y\ (\text{CVP}) = 2.0282\,X + 184.7118$$

(X = body length).

The coefficient of correlation of 0.68 shows a close relationship.