Magnesium Deficiency in Pregnancy and its Effects on the Fetus

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Zusammenfasssung

Die verfügbaren Daten über Magnesium-Gehalte in Blut und anderen Körperflüssigkeiten (Speichel, Fruchtwasser) schwangerer Frauen und menschlicher Föten werden zusammengestellt. Im allgemeinen besteht Übereinstimmung darin, daß das Plasma- bzw. Serum-Mg während der Gravidität abnimmt, während der Gehalt der Föten, vor allem im letzten Trimester, ansteigt.
Studien mit experimentell während der Schwangerschaft erzeugtem Mg-Mangel zeigen, daß Mg-Mangel teratogen wirkt und zu Problemen bei der Geburt und später bei der Rückbildung der Uterusmuskulatur führt. Relativ leichter Mg-Mangel während der Schwangerschaft verursachte schwere Anämie bei den Föten, ohne Beeinflussung des mütterlichen Blutstatus.
Wenig ist bekannt über Zusammenhänge zwischen Mg-Mangel und gestörter fötaler Entwicklung beim Menschen; diese wichtige Frage muß weiter untersucht werden.

Summary

The available data are summarized concerning magnesium levels in blood and other fluids (saliva and amniotic fluid) in pregnant women and magnesium content in human fetuses. There is, in general, agreement that magnesium concentration in plasma or serum declines during pregnancy, while magnesium content of fetuses increases, especially during the last trimester.
Experimental studies of magnesium deficiency during pregnancy show that deficiency of this element has teratogenic effects, as well as leading to problems of parturition and delayed post-partum uterine involution. Relatively mild magnesium deficiency during pregnancy caused severe anemia in the fetus, with no hematological effects in the mother.
There is very little information on magnesium deficiency in relation to abnormal fetal development in humans; research is needed on this important question.

Resumé

Nous avons résumé les données disponibles concernant les taux du magnésium dans le sang et d'autres liquides (salive et liquide amniotique) chez les femmes enceintes et la teneur du magnésium chez les foetus humains. Il existe, de façon générale, un accord sur le fait que la concentration du magnésium dans le plasma ou le sérum s'abaisse au cours de la grossesse, alors que la teneur en magnésium des foetus s'accroît spécialement au cours du dernier trimestre.
Des études expérimentales du déficit magnésique au cours de la grossesse montrent que le déficit de cet élément présente des effets tératogènes et qu'il entraîne aussi des problèmes de parturition et une involution utérine différée dans le post-partum. Un déficit magnésique relativement bénin au cours de la grossesse a provoqué une anémie grave dans le foetus, sans effets hématologiques chez la mère.
Il existe très peu d'information sur le déficit magnésique en rapport avec le développement foetal chez l'homme; une recherche sur ce point important est nécessaire.

I. Introduction

The subject of magnesium deficiency in pregnancy and its effect on the offspring was reviewed in 1971 at the First International Symposium on Magnesium Deficiency *(Hurley, Vittel,* 1971). At that time, it was recognized that magnesium levels in blood plasma or serum are lower in pregnant than in nonpregnant women, but the physiological significance of this observation was not clear. It was also recognized that magnesium is essential for normal development of the fetus, but very few studies, either in experimental animals or in humans, had been published. A few studies in rats showed that magnesium deficient diets during pregnancy caused death and malformation of the young, or under less severe conditions, fetal anemia.
Since the publication of the First International Symposium on Magnesium, relatively few additional studies have been reported concerning this subject. The present review will attempt to summarize present knowledge, with special emphasis on the work which has appeared during the past ten years.

II. Tissue magnesium in pregnant women and fetuses

Magnesium in blood

Few studies have been published in the last ten years on the blood plasma or serum levels of magnesium during pregnancy in women. *Dale* and *Simpson* (1972) studied serum magnesium concentration in 23 women who were more than 35 weeks pregnant and found it to be significantly lower than that in non-pregnant women. *Watney* et al. (1971) measured serum magnesium in Asian, Caucasian, and West Indian women in England at their first antenatal visit (10 to 20 weeks) and at 29 and 36 weeks of gestation. No decline with length of gestation was apparent. Difference in the values for the three groups did not reach statistical significance, but they were highest at each sampling in the Asian mothers (N = 9 to 51 samples per value) the opposite of the trend for calcium.
Olatunbosun et al. (1975) found a decline in serum magnesium during the course of pregnancy in Nigerian women, with a rapid rise during the postpartum period to above nonpregnant control values.
Reitz et al. (1977), measured serum magnesium in women from 11 to 40 weeks of gestation. They found no significant differences among various periods of pregnancy. However, they did observe a significantly lower concentration of maternal serum magnesium at delivery (1.81 ± 0.02 mg/dl) than at 28—40 weeks' gestation (1.97 ± 0.03 mg/dl). A summary of the data reported in the literature on magnesium in blood serum or plasma of pregnant women is presented in Table 1.

Tab. 1: Magnesium in Blood Serum or Plasma of Pregnant Women.

Reference	Serum or Plasma Magnesium			
		Pregnant		
	Nonpregnant	No. of Women	Period of Gestation	Magnesium
	mg/dl			mg/dl[a]
Krebs and Briggs, 1923	—	17	8 to 40 wks.	Varied from 2.1 to 2.7
Plass and Bogert, 1923	2.3	40	1 to 40 wks.	Decreased from 2.3 to 2.1
Zaharesco-Karaman, 1936a	2.5	75	1st to 9th month	General increase to 2.9, with decrease in 6th month to 2.3
Wolff et al., 1937	1.9	22	2nd to 9th month	Increased from 1.2 to 1.6
Hall, 1957	2.3	294	11wks. to term	Some decrease, low of 2.0
DeJorge et al., 1965a	2.6	99	2nd month to term	Decreased from 2.0 to 1.5
DeJorge et al., 1965b	2.6	139	1st month to term	Decreased from 2.3 to 1.7
Celli Arcella, 1966	2.6	159	The 3 trimesters	Decreased to 2.2
Lupi et al., 1967	2.1	25	Term	1.7
Watchorn and McCance, 1932	2.7	12	Unspecified	2.4
Rosner and Gorfien, 1968	2.2	27	Unspecified	1.8
Mahran and Hanna, 1968	—	30	3rd Trimester	2.2
Stefanini et al., 1968	2.2	15	9th month	1.9
Dawson et al., 1969a	—	244	10th wk. to term	Decreased from 3.2 to 2.7
Lim et al., 1969	2.0	105	3rd trimester	1.7
Watney et al., 1971				
Asian	—	16	10—20 wks.	1.9
	—	34	29	1.9
	—	34	36	1.9
Caucasian	—	9	10—20	1.8
	—	36	29	1.8
	—	48	36	1.9
West Indian	—	14	10—20	1.8
	—	14	29	1.8
Dale and Simpson, 1972	2.1	23	> 35 wks.	1.8
Nusbaum and Zettner, 1973	—	15	11—19	1.6
Olatunbosun et al., 1975	1.5	4	3 months	1.5
		21	4	1.6
		39	5	1.6
		30	6	1.7
		29	7	1.5
		34	8	1.3
		36	9	1.0
Reitz et al., 1977	2.0	40	8—13	2.0
		30	14—19	2.2
		40	20—27	2.0
		40	28—40	2.0

[a]The data of the few authors giving their results as mEq/l have been converted to mg/dl.

The magnesium in maternal serum or plasma has also been compared with magnesium in the cord blood of fetuses or newborn infants at delivery. These studies are summarized in Table 2. In most cases, maternal serum magnesium was lower than that in the infants. The plasma magnesium concentration of full term newborn infants was compared with that of prematures by *Chabrolle* et al. (1977). They found that the plasma magnesium level of premature female infants was significantly higher than that of full term girls, while between premature and full term newborn boys, there was no difference. No explanation for the elevated plasma magnesium of premature female infants is at hand.

Magnesium in saliva and amniotic fluid

Magnesium concentration has also been reported in the saliva of pregnant women. *Kayavis* and *Papanayotou* (1976) reported that the salivary magnesium concentration of pregnant women was significantly higher than that of non-pregnant women. The magnesium concentration of amniotic fluid has been analyzed. *Nusbaum* and *Zettner* (1972) analyzed magnesium in the amniotic fluid of pregnant women and compared it with maternal serum. Magnesium concentration was found to be significantly lower in amniotic fluid than in maternal serum. *Favier* et al. (1972) also measured magnesium concentration in amniotic fluid (Table 3).

Tab. 2: Magnesium in Maternal and Fetal Blood Serum or Plasma

Reference	No. of Women	Serum or Plasma Mg[a] Maternal	Fetal
		mg/dl	mg/dl
Bogert and *Plass*, 1923	40	2.0	2.1
Zaharescu-Karaman et al., 1936b	30	1.85	2.4
Wallach et al., 1962	3	2.0—2.1	Similar[b]
Brunelli et al., 1966		Cord blood lower than maternal blood until 37th week, then similar	
De Jorge et al., 1966	50	2.2	2.3(3)
Kiryushchenkov, 1965	10	2.7	2.6(2)
Reitz et al., 1977	30	1.81±0.02	1.92±0.02[b, c]

[a]The data originally expressed as mEq/L have been converted to mg/dl.
[b]Newborn.
[c]Significantly different from maternal.

Tab. 3: Magnesium in Human Amniotic Fluid

Reference	No. of Women	Mg in Amniotic Fluid
		mg/dl
Nusbaum and Zettner, 1972	20	1.13±0.42
Favier et al., 1972	59	1.3±0.62

Magnesium content of fetuses

There have been no new studies on the magnesium concentration of fetal tissues during the past ten years. *Widdowson* (1974) has summarized the magnesium concentration of the human fetus (Table 4).

Tab. 4: Magnesium in Developing Human Fetus

Body Weight	Approx. Fetal age	Total in body	Magnesium Per kg. Fat-free tissue
g	weeks	g	g
30	13	0.003	0.10
100	15	0.01	0.10
200	17	0.03	0.15
500	23	0.10	0.20
1,000	26	0.22	0.22
1,500	31	0.35	0.24
2,000	33	0.46	0.24
2,500	35	0.58	0.25
3,000	38	0.70	0.27
3,500	40	0.78	0.27

Adapted from Widdowson, 1974

III. Magnesium status of pregnant women

Maternal magnesium requirements increase during pregnancy because of the synthesis of new tissue, both fetal and maternal. Balance studies have suggested that there is an accumulation of magnesium by the pregnant woman from approximately 1 g at the third lunar month of gestation to approximately 11 g at the 10th lunar month (*Macy* and *Hunscher*, 1934). The needs of the fetus for magnesium are especially great during the third trimester because of its rapid rate of growth and the increasing concentration of magnesium in its tissues (Table 4). Although there is general agreement that magnesium is important for pregnant women, evaluation of its status has presented problems.

Caddell et al. (1973) have developed a method which appears to provide a measure of magnesium status. A solution of magnesium sulfate was injected intramuscularly, and its retention (as measured by urinary excretion) was determined. (A higher retention would indicate lower magnesium status). This test demonstrated significantly higher retention of magnesium in postpartum than in nulliparous women. However, some of the postpartum women retained very little magnesium, suggesting that their needs for magnesium during pregnancy had been met.

The possible relationship of magnesium nutrition to toxemia of pregnancy has received considerable discussion, but there is little actual evidence at the present time (*Hurley*, 1971; *Seelig*, 1980).

IV. Magnesium in relation to human congenital abnormalities

Although magnesium deficiency in rats causes congenital abnormalities (see below), only a few reports have been found concerning the possible relationship of congenital abnormalities in humans to magnesium metabolism or nutrition. *Mameesh* et al. (1978), in Kuwait, measured the plasma magnesium concentration of 20 women who had delivered low birth weight infants. They did not find it to be significantly different from women whose infants were of normal birth weight.

The possible relationship of the magnesium concentration of drinking water to malformations of the central nervous system (CNS) has been studied. In South Wales, where a significant negative correlation was found between the incidence of malformations and the hardness of the water supply, *Morton* and *Elwood* (1974) did not find a correlation between the CNS malformation rate and the magnesium concentration of the water, although other elements were negatively correlated. In Canada, however, *Elwood* (1977) found a negative association between the concentration of magnesium in the drinking water and the mortality rate from anencephalus. The significance of this observation and its relationship to other factors in the etiology of CNS malformations is as yet not clear, and should be further investigated.

V. Experimental magnesium deficiency in pregnancy

Teratogenic aspects

Experimental magnesium deficiency in pregnancy and its effects on fetal development have been studied most extensively in rats.

Tufts and *Greenberg* (1938) in a study of magnesium deficiency in nonpregnant rats, concluded that a diet containing 5 mg of magnesium per 100 g was on the borderline of the dietary requirement. They also made some fragmentary comments on the effects of a magnesium deficient diet during pregnancy. Although little information was given, the author's observations indicated that magnesium was necessary for normal pregnancy. A preliminary report by *Zoumas* and *Barron* (1969) suggested that an inadequate amount of magnesium during pregnancy and lactation affected the chemical composition of the brain in the offspring of rats.

In our laboratory (*Hurley* et al., 1976a), normal adult Sprague-Dawley female rats were fed a purified diet, either deficient in magnesium (0.2 mg magnesium/100 g diet) or complete (control diet, 40 mg/100 g diet) throughout pregnancy, that is, from day 0 to day 21 of gestation. The diets were identical except for their magnesium content. The diets contained either casein or isolated soybean protein; some groups were fed these diets during different periods of gestation. The plasma magnesium concentration of rats fed the magnesium deficient diets fell very rapidly after the institution of the deficiency regimen. As early as one day after the diet was started, the plasma magnesium concentration had fallen by almost 50%, and on the fourth day it had fallen to about one-third of the starting concentration.

The magnesium deficient diet had very profound effects on reproduction (Table 5). When the deficient diet was given throughout pregnancy, 100% of the implantation sites showed resorptions. When the dietary deficiency was limited to days 6 to 14 of gestation, 89% of the implantation sites in females given the soybean diet were resorbed, and 22% of the living full-term fetuses were malformed. When the diet was fed only from day 6 to day 12 of gestation, 17% of the implantation sites were resorbed and 16.5% of the live young were malformed. There was a wide variety of malformations, but those of highest frequency were syndactyly, tail and lung malformations, diaphragmatic hernia, and hydronephrosis. With casein as the protein source in the purified diet, all of the implantation sites were resorbed when the diet was fed throughout gestation. When this diet was fed from day 6 to day 14 of gestation, 49% of the implantation sites were resorbed and 6.8% of the full-term fetuses were malformed. When the deficient diet was fed from day 6 to day 12, only 5% of the implantation sites were resorbed, and none of the fetuses were malformed.

Dietary magnesium deficiency also caused a lower than normal maternal weight gain, possibly associated with reduced food consumption. Short periods of magnesium deficiency during pregnancy had a lesser effect on maternal plasma magnesium concentration at term and on food consumption, but still dramatically influenced the ability of female rats to maintain pregnancy. Diets containing either casein or soybean protein appear to have the same effects, although the casein fed rats were not as severely affected. The rapid effects of dietary magnesium deficiency on the developing rat embryo are probably related to the low maternal plasma level that occurred after only a few days of dietary deficiency.

Schwartz and her colleagues (*Wang* et al., 1971) have also studied the effect of magnesium deficiency during pregnancy. When pregnant Sprague-Dawley rats were fed a diet containing 8 mg magnesium/100 g, there was a high incidence of stillbirths and over 90% of the offspring alive at birth died during the first week of life. The litter size was not affected, but body weight and magnesium content of the newborn young were significantly lower than in controls. It is noteworthy that when the same diet was fed during lactation, the magnesium deficiency affected the maternal animal more seriously than it did the offspring, in contrast to the effect of the deficient diet during pregnancy.

Studies by *Günther* and his co-workers (1973) confirmed the deleterious effects of magnesium deficiency on the offspring of pregnant rats. With a casein-containing diet deficient in magnesium (1.2 mg/100 g), these workers found many resorptions, the frequency of

Tab. 5: Effect of Magnesium Deficiency on Fetal Development in Rats

Experimental Group	Females	Plasma Mg	Fetuses			Total Implantations	
			No.	Body Wt.	Malformed[a]	Resorptions	Affected Sites
	No.	mg/dl		g	%		
Control (40 mg/100 g)							
Soybean diet	14	2.4	162	5.3	0	5.3	5.3
Casein diet	13	2.4	128	5.3	0.8	7.2	8.0
Magnesium Deficient							
Soybean diet (0.2 mgMg/100 g)							
Days of gestation							
0—21	14	0.88[c]	0	—	—	100	100
6—14	23	2.7[d]	32	4.5[c]	22	89	92
6—12	29	2.3	284	4.9[c]	17	17	31
Casein diet (0.3 mgMg/100 g)							
Days of gestation							
0—21	8	0.77[f]	0	—	—	100	100
6—14	12	2.3	74	4.7[f]	6.8	49	53
6—12	9	2.1[f]	95	4.9[f]	0	5.0	5.0

[a]Live fetuses malformed
[b]Fetuses malformed plus resorptions
[c]Significantly different from soybean diet control, $P < 0.001$
[d]Significantly different from soybean diet control, $P < 0.01$
[e]Significantly different from casein diet control, $P < 0.001$
Adapted from Hurley et al., 1976.

which depended upon the timing and duration of the deficiency. If the dietary deficiency was imposed from day 7 to day 15, 77% of the implantation sites were resorbed. With as little as four days of deficiency, from days 8 to 12, 13% of the embryos were resorbed. Magnesium deficiency after this time had relatively few effects. However, in all of the groups tested, the total number of litters was quite small. Only a few of the fetuses alive at term showed malformations. The 12-day old embryos of females fed the magnesium deficient diet from day 0 to day 12 had a significantly lower content of potassium than was found in controls. When rats were given the magnesium-deficient diet (1.2 mg/100 g) from day 5 to day 12 of pregnancy, their offspring showed high neonatal mortality and abnormal histology in the brains of the newborns. Necrosis and reduction of thickness in the brain cortex, as well as hydrocephalus was observed. Newborn rats showed swelling of the mitochondria and loss of lipid inclusions in the brown adipose tissue. The high neonatal mortality of these animals may be related to these abnormalities, since the brown adipose tissue plays an important role in temperature regulation in the newborn.

Mineral composition of tissues

The plasma magnesium levels of pregnant rats fed a commercial stock diet and their fetuses were measured from 16.5 to 21.5 days of gestation and during the first week after birth (*Garel* and *Barlet*, 1974). Plasma magnesium concentration was invariably higher in the fetuses than in the mother. The highest concentration was seen in the 16.5 day fetus (2.92 mg/dl as compared with 1.76 mg/dl in the mothers).

The concentrations of magnesium, calcium, and zinc of maternal and fetal tissues at term were measured in rats given a diet containing 5 mg magnesium/100 g of diet (mild deficiency) during pregnancy (*Hurley* et al. 1976). In females fed the magnesium deficient diet, kidney calcium was higher and femur magnesium was lower at term than in controls. The magnesium content of the fetuses, as well as its concentration in the ash, was lower in those from magnesium deficient rats than in controls. Calcium concentration in the ash, however, was unchanged in the magnesium deficient fetuses. The zinc content in these fetuses, both total zinc per fetus and its concentration in the ash, were significantly lower in magnesium deficient fetuses than in controls. These results led us to examine the possibility of an interaction between magnesium and zinc in producing congenital malformations. We therefore measured the zinc concentration in fetuses of rats fed purified diets containing various amounts of magnesium and zinc. The concentrations of magnesium, calcium, and iron were also measured. Preliminary results are shown in Table 6. As in the earlier work, the magnesium concentration of fetuses from females fed a magnesium deficient diet was lower than normal. The zinc concentration, however, was unaffected by the maternal dietary magnesium. In contrast, both calcium and iron were higher in fetuses of magnesium deficient fetuses than in the other groups (*Keen* et al. In preparation).

Tab. 6: Concentration of Mg, Ca, and Fe in Fetal Body at Term[a].

Diet[b] Mg	Zn	Mg	Zn	Ca	Fe
mg/100g	ppm	mg/g dry wt.	µg/g dry wt.	mg/g dry wt.	µg/g dry wt.
200	100	1.32	124	18.9	424
40	100	1.21	120	16.9	426
5	100	0.88	129	26.6	547
5	1000	1.05	126	20.1	531
40	1000	1.34	147	17.8	425

[a]Number of fetuses per group varied from 3 to 8
[b]Normal dietary concentrations are 40 mg/100 g for magnesium, and 100 ppm zinc.
Adapted from Hurley et al., 1976.

Fetal anemia

With a relatively mild deficiency of magnesium (2.5 to 5.0 mg/100 g), the incidence of resorptions was high and over 40% of the fetuses alive at term showed malformations, including cleft palate, micrognathia, clubbed feet, syndactyly short and curly tail, and herniation. In addition, the fetuses alive at term were edematous and severly anemic (*Cosens* et al. 1977). The number of red blood cells and the concentration of hemoglobin were markedly reduced in full-term fetuses of females fed a magnesium deficient diet; hemoglobin was less than half the normal level. This was in contrast to the effects of the magnesium deficiency on maternal hematology; all of these parameters were normal in the magnesium deficient dams. In neither the mothers nor the fetuses was the concentration of magnesium in the red blood cells reduced by dietary deficiency of the element (Table 7).

Tab. 7: Effect of Magnesium Deficient Diet on Blood of Pregnant Rats at Term[a].

	Control Diet[b]	Deficient Diet[c]
Maternal		
No. of rats	13	13
Red blood cells, × 10^6	5.2	4.9
Packed cell volume, %	36.8	36.6
Hemoglobin, g/dl	10.4	10.7
Fetal		
No. of litters	5	5
Red blood cells, × 10^6	1.6	1.0[d]
Packed cell volume, %	30.8	25.4
Hemoglobin, g/dl	8.0	3.6[d]

[a]Diets fed days 0—21 of pregnancy.
[b]Contained 40 mg Mg/100 g; casein diet.
[c]Contained 2.5 mg Mg/100 g; casein diet
[d]Significantly different from control, $P < 0.01$
Adapted from Cosens et al., 1977

Maternal dietary magnesium deficiency thus had profound effects on fetal hemotopoiesis. In magnesium deficient fetuses, erythropoiesis was significantly greater than normal in liver, adrenal, and spleen. Light microscopy showed no differences in red cell maturation, but electron microscopy of magnesium deficient fetal liver did show differences in the stage of maturation. Red blood cells appeared to stop development at the reticulocyte stage, after nuclear extrusion, with many organelles and membranes remaining in the cells. Many red blood cells near maturation or matured were bizarre in shape and contained vacuoles or holes. Few of these cell types were found in fetal liver from control fetuses.

Stained and unstained smears of peripheral blood revealed extreme alterations in red cell morphology characterized by abnormality in size, shape, amount of hemoglobin, membrane conformation, and the number and type of nucleated red cells. There was an obvious macrocytosis associated with numerous microcytes and red cell fragments. Scanning electron microscopy of peripheral red blood cells from magnesium deficient fetuses showed abnormalities of shape, consisting of bud-like excrescences and irregular, small, pointed fragments, excessive dyscocytic forms, blebs or protrusions, and holes (Figure 1a, b). These flattened discocytic forms were due not to vacuoles, but to absence of hemoglobin in the center of the enlarged, flattened, red blood cells.

Plasma protein concentration was also significantly lower in fetuses from magnesium deficient rats than in controls and is probably related to the extreme edema characteristic of these animals. In maternal blood, however, magnesium deficiency did not reduce the concentration of plasma protein. Magnesium deficiency also did not influence the electrophoretic pattern of hemoglobin in either mothers or fetuses.

The anemia of magnesium deficient fetuses is hemolytic in nature and appears to be the direct result of red cell malformation. The morphological features of this anemia are consistent with the hypothesis that the most important factor in its development is abnormality of the red cell membrane due to magnesium deficiency. The collapse of membrane to produce folds and grooves and "holes" is quite apparent by interference and scanning electron microscopy and is consistent with the work of *Elin* (1980) on the role of magnesium in membrane integrity. Transmission electron microscopy establishes that there are no vacuoles underlying the "holes", merely a circular collapse of membrane (Figure 1c).

Magnesium deficiency also produced abnormalities of chromosomes (*Bell* et al. 1975). Cells of both maternal bone marrow and fetal liver showed significantly more chromosomal anomalies than did those of controls. Chromosomal aberrations occurring in highest incidence were terminal deletions and fragments. "Stickiness" of chromosomes was also observed in cells from magnesium deficient mothers and fetuses, as had previously been found in magnesium deficient plants. Magnesium may thus be necessary for the integrity of chromosome structure; however, the relationship of the chromosomal anomalies to congenital malformations is not known.

The fetal anemia produced by magnesium deficiency was also reported by *Cohlan* et al. (1970). Although these investigators did not observe congenital malformations in the offspring of magnesium deprived rats, they did report low fetal body weight at term, low plasma magnesium in both mothers and fetuses, and low hemoglobin and hematocrit in the magnesium deficient fetuses.

Parturition and uterine involution

Magnesium deficiency during pregnancy also has profound effects on the process of parturition and on uterine involution in the rat. *Rayssiguier* and his colleagues (1979) have reported that in rats fed during pregnancy a casein diet containing 11 mg magnesium/100 g, the plasma magnesium concentration of the dams was lower than in controls, but the number of parturient females and their weight at parturition was not affected by magnesium deficiency. Neither was there any effect on the weight or the size of the litters. The number of stillbirths was the same as in controls and no malformed fetuses were reported.

However, there were very marked effects on the process of parturition. The birth process in the rat begins with the contraction phase. The periodic waves of contractions of the abdominal muscles were noted more often in the controls than in the deficient rats. In addition, the contractions were of much shorter duration in the defiecient females. The duration of the birth process was also significantly longer in deficient than in control females (Table 8).

Tab. 8: Effect of Magnesium Deficiency on Parturition in Rats[a]

	Control Diet[b]	Deficient Diet[c]
Number of rats	13	18
Duration of contractions, min.[d]	56	21[e]
Birth process, min.[f]	103	119[e]

[a]Diets fed throughout pregnancy
[b]Contained 150 mg Mg/100 g
[c]Contained 11 mg Mg/100 g
[d]From first abdominal contraction observed to delivery of the first fetus
[e]Significantly different from control
[f]From first appearance of fetus to taking a lactational position
Adapted from Rayssiguier et al., 1979

In the postpartum period, the uterine weight of magnesium deficient rats was greater than that of controls, and this was probably related to the less rapid decrease in hydroxyproline concentration of the uterus in magnesium deficient females (Figure 2). The concentration of uterine hydroxyproline in controle rats increased between the day of birth and the first day

postpartum, but then declined by day 4. In contrast, in magnesium deficient females, uterine hydroxyproline concentration continued to increase and was significantly higher than in controls on day 4 and day 7 postpartum. However, when the magnesium deficient females were given a magnesium supplemented diet at parturition, the uterine hydroxyproline concentration fell to the normal level by day 4. Since hydroxyproline concentration is a measure of collagen, these results suggest that collagen disappears very slowly from the postpartum uterus in magnesium deficiency. This may be brought about by some effect of magnesium deficiency on collagenase activity or on synthesis or release of collagenase. It is also of interest that the concentration of magnesium in the uterus was significantly lower than normal in magnesium deficient females fed the deficient diet during pregnancy and lactation, while at the same time the concentration of calcium in the uterus was higher. This observation is in contrast to that in bone, where there was less magnesium than in controls, but no change in calcium concentration.

VI. Concluding remarks

It is well established that magnesium is essential for the normal development of the fetus. Experimental studies with rats have demonstrated that a diet deficient in this element, although adequate in all other nutrients, causes a variety of problems, depending on the severity of the deficiency. These include fetal death and malformation, fetal anemia, difficulty of labor, and neonatal abnormalities. The relationship of these effects of magnesium deficiency to problems of pregnancy in humans is at present unclear, but should be explored.

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