Association of Low Intake of Milk and Vitamin D with Decreased Birthweight

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It's always nice to come to a conference and find out that you are speaking after someone who has presented data that is in tandem with your own. But I am going to give a slightly different perspective on this relationship, using Canada as a case study for the presentation of this data because it provides a unique environment, I think, relative to what some other communities and countries are experiencing.

Milk Consumption during Pregnancy

- **Widespread recommendation to restrict milk by both health professionals and lay press**
- **Only one-third of Canadian women consume milk**
- **Most (>85%) take prenatal supplements**

In Canada there is a widespread recommendation by both health professionals and the lay press to restrict milk consumption. We surveyed the lay press, and probably 90 percent of all lay press articles giving advice to women during pregnancy advise not to drink milk during pregnancy. They also advise not to drink milk during lactation. Our nursing, pharmacy, and medical professionals support this advice.

Only one-third of Canadian women, across all ages and all groups, consume milk at this point in time. In contrast, almost 97 percent of all men consume milk. So we have a gender difference in our milk consumption pattern. In the Danish study just presented, I recall that about 1 percent of women consumed less than 1 glass of milk per day. In Canada 14 percent of women restrict milk during pregnancy. They give about 5 reasons for restricting milk besides the advice of their health professional. Number 1 is to lower their fat intake, number 2 is to avoid diabetes, number 3 is to avoid allergy, number 4 is to avoid colic, and number 5 is a self-diagnosis of lactose intolerance, which they report at a rate that is higher than the population average. Interestingly, on average, 85 percent of Canadian women take vitamin supplements that include calcium and Vitamin D and in our study it was 97 percent. So all of our non-milk restrictors were taking a vitamin supplement, but fewer of our milk restrictors, who need supplements, were taking them.

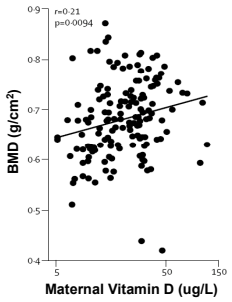
Vitamin D Status in Term Infants at Birth by Location and Season

Authors	Year	Location	Vitamin D*
Kuroda et al	1981	Japan	Summer > Winter (18.9 ± 8.4 vs 8.8 ± 3.4)
Nehama et al	1987	Israel	Fall < Spring (18.1 ± 1.3 vs 11.3 ± 1.0)
Namgung et al	1994	Ohio	NS Summer vs Winter (24.2 ± 1.3 vs 21.6 ± 2.7)
Namgung et al	1998	Korea	Summer > Winter (12.0 ± 6.0 vs 4.3 ± 3.0)
Weiler et al	2005	Canada	36% < 19 ± 6 vs 39.7 in control

* Values are mean ± SD except Nehama (1987) and Namgung (1994) which are mean ± SE
Values are ng/mL- Weiler is nmol/L

This is some of the background information we had at the time we began our study. Here you see that in Japan, Korea and Canada, in general, the Vitamin D status is higher in the summer than the winter, and in Israel it is higher in the spring than the fall. And the study in Canada indicates that 36 percent of all infants have 19 nanomoles per liter of circulating Vitamin D versus the control value norm of 39.7. In the other studies these measures are expressed in nanograms per milliliter, which if doubled provide an approximate relationship to nanomoles per liter. So all of the studies are pretty much seeing a seasonal difference over the course of one year in terms of circulating levels of Vitamin D at birth.

Vitamin D exposure *in utero* relates to bone mass in childhood at 9 years



Javaid et al, Lancet 367;36, 2006.

The recent Javaid study indicates that there is a relationship between Vitamin D exposure in utero and bone mass in childhood at nine years of age. And there is this belief now that is growing in the literature that there is probably some kind of imprinting that might be going on *in utero* with regard to Vitamin D.

Hypothesis

- **Lower intake of fortified milk by pregnant women living at northern Canadian latitudes is associated with reduced:**
  - **Birth weight**
  - **Birth length**
  - **Head circumference**

Milk was fortified with Vitamin D in 1965 in Canada in recognition that we had a very large problem with rickets. It was done in the 1940s in the US. The second issue that emerged in Canada in the early 1990s was the growing recognition that we have a national epidemic of Vitamin D deficiency. This does not only affect pregnant women. In any population we measure, including Inuit, from infants through adults, we will find Vitamin D deficiency. Most of Canada is situated in northern latitudes where from about late October to late March, early April, there is no conversion of the precursor in the skin to active Vitamin D. So we need to have a dietary Vitamin D source during the winter months. And, again, most women aren't taking in this dietary source. So we decided to investigate whether the offspring of Canadian women that restrict milk intake would have evidence of reduced birth weight, birth length, or head circumference.

Characteristics of Study Population

	Mean		*p* value
	NR-No restriction *n* = 207	R-restrictors *n* = 72	
Age at delivery , yr	31.2	30.0	0.11
Height, m	1.66	1.65	0.053
Weight before pregnancy, kg	63.9	62.0	0.25
Body mass index, kg/m^2	23.2	22.9	0.61
Gestational weight gain, kg	16.8	15.9	0.32
Smoking, #	12	4	0.97
University education, #	94	37	0.33
Vitamin or mineral supplement use, #	201	38	0.050
Birth weight, g	3530	3410	0.07
Length, cm	51.4	51.1	0.46
Head circumference, cm	34.6	34.3	0.19

We went to Calgary, Alberta, the sunniest city in Canada. There are three university hospitals there, and we were able to identify a group of women that did not restrict milk intake and a group of woman that actively restricted milk intake. Our study population is comprised of what I would describe as healthy Canadian women. Their ages at delivery were, on average, in line with most Canadian women who deliver between ages 26 and 36. We see normal heights, normal pre-pregnancy weights, normal body mass indices and appropriate gestational weight gains in line with the recommendations that we have. We have very little smoking in our study population. Most of our women were university educated, and if you include the equivalent of junior college, over 90 percent of the population had some form of university education. The majority was taking vitamin supplements. But what was interesting is more vitamin supplement consumption was occurring in those that did not restrict milk than in those that did restrict milk and this was part of our concern. When health professionals were making the recommendation not to drink milk, were they also suggesting that women take vitamin D supplements? The vitamin supplementation recommendation didn't appear to be universal.

Length and head circumference were not different between the groups but note the difference in birth weight, 3,530 grams versus 3,410 grams. That is a 120-gram difference between the two groups with a P value of 0.07. Is it statistically significant? Technically, no but consider the impact of smoking on pregnancy. Birth weight is 150 grams lower in the offspring of mothers who smoke. So in terms of fetal growth, the magnitude of the effect of restricting milk intake during pregnancy is about the same as smoking during pregnancy.

Dietary Intakes

NUTRIENTS	Mean		*p* value
	NR *n*= 207	R *n*= 72	
Energy, kcal	2465 ± 501	2424 ± 664	0.06
Fat, g/d	83 ± 25	87 ± 33	0.33
Protein, g/d	106 ± 27	95 ± 35	0.014
% < EAR	9.2	20.8	0.009
Riboflavin, mg/d	6.5 ± 4.8	6.6 ± 6.1	0.80
% < EAR	0	0	
Calcium, mg/d	1864 ± 497	1726 ± 765	0.16
Vitamin D, ug/d	13.1 ± 4.5	7.9 ± 4.7	<0.001

Now we will look at the issue of dietary intakes within our population. We did 24-hour recalls, three to four times during the course of the pregnancy, as early as the tenth week post conception. And you will notice here that the energy intake between our restrictors and nonrestrictors was comparable, but slightly higher in our nonrestrictors. Fat intake was in line with recommendations. The average Canadian takes in about 30 percent fat, which is comparable to 31 percent in our population. Protein intake was significantly different at 106 grams in our nonrestrictors and 95 grams in our restrictors, but well above the levels suggestive of protein deficiency. However, the percentage of women in the restrictor group who were below the EAR (estimated average requirement) for protein was much higher than it was in our nonrestrictor group. So there's definitely a group of women who take in milk to meet their protein requirements. There were no differences in riboflavin or calcium, but vitamin D was different between the two groups. Note that both vitamin D levels, although presenting a statistically significant difference, are greater than the general recommendations now at 5 ug/day. So both groups of women were getting adequate intakes of Vitamin D. However, in the restrictor group the bulk of that was coming from their supplements, not from their diet. But, again, they were meeting the vitamin D recommendations as currently expressed.

Regression Model for Infant Birth Weight: Milk Intake (n=269)

CHARACTERISTIC	Birth Weight	
	β coefficient (95% CI)	*p* value
GESTATIONAL		
Weight gain, kg	13 (4 to 22)	0.005
Age, wk	24 (1 to 47)	0.035
MATERNAL		
Age, yr	-13 (-24 to -3)	0.012
Height, cm	83 (32 to 133)	0.001
Education, yr	112 (7 to 218)	0.036
Body mass index, kg /m^2	24 (11 to 17)	<0.001
Milk intake, L	9 (3 to 17)	0.016
Cups	41 (13 to 75)	
Vitamin D intake, ug/d	NA	

The first regression model we did was to determine if, indeed, the effect of milk restriction entered as a significant predictor of birth weight. We used the same covariates in the restriction model, but in place of the milk intake in cups, we substituted a variable for "restriction" and we found that restricting milk intake had a significant impact on predicting birth weight. Interestingly, this model came up with 120 grams, which was the difference we found in the birth weight between our two groups. In this particular framework, controlling for everything that we have here, what's very important to note is that milk intake was a significant predictor of birth weight. For every cup of milk the women consumed daily they added 41 grams to the birth weight of their offspring.

Regression Model for Infant Birth Weight: Vitamin D Intake (n=269)

CHARACTERISTIC	Birth Weight	
	β coefficient (95% CI)	*p* value
GESTATIONAL		
Weight gain, kg	13 (4 to 22)	<0.001
Age, wk	25 (2 to 48)	0.032
MATERNAL		
Age, yr	-14 (-25 to -3)	0.008
Height, cm	87 (37 to 137)	<0.001
Education, yr	111 (6 to 217)	0.038
Body mass index, kg /m^2	26 (13 to 39)	<0.001
Milk intake, L	NA	
Cups	NA	
Vitamin D intake, ug/d	11 (1 to 20)	0.029

In the second model we evaluated all nutrients one might expect to be predictive, protein, riboflavin, calcium, and energy. None of the nutrients except Vitamin D showed up as a significant predictor of birth weight. For every microgram per day consumption of Vitamin D, the women increased the birth weight of their offspring by 11 grams.

Study Conclusions

- Restriction of milk lowers infant birth weight (3410 g vs 3530 g) in healthy women
- Each cup of milk raises birth weight by 41g
- Each ug of vitamin D increases birth weight by 11g
- Pregnant women at northern latitudes may require more foods fortified with Vitamin D and/or supplements
- Other nutrients?
  - Protein
  - Fats / fatty acids

So our conclusions were that the restriction of milk lowers infant birth weight by 120 grams. While there's a big debate as to whether that 120 grams is going to be significant or not, it is very similar to what they saw in the Danish study. Each cup of milk raises birth weight by 41 grams. Each microgram of Vitamin D increases birth weight by 11 grams.

So the choice in the Canadian population, which we're trying to push in public health messages, is drink milk or take a Vitamin D supplement, but you need to be doing one or the other, or getting more fish, seal liver, or polar bear liver in your diet, which outside of the Inuit population, are not regularly consumed. In recent times we now have fortified yogurt, margarine, rice and soy beverages and ready to eat cereals. So we clearly want to be making the recommendation in the Canadian context that pregnant women at northern latitudes may require more foods fortified with Vitamin D and/or supplements.

The question remains are there other nutrients that may be playing a role in this? We did not see one with protein; however, we did see a relationship with zinc and we know there is an association between protein consumption and zinc so we could be picking up some contribution from zinc in this equation. The other one, that is emerging that is quite interesting for us, is the fatty acids. I am currently looking at the vitamin D content and other components in the amniotic fluid of pregnant women. Interestingly, C 15:0, which is a biomarker of dairy product consumption, is also coming up in our fatty acid analysis as a predictor of birth weight, inversely for small for gestational age and positively for large for gestational age. So I believe there is probably a range of nutrients that we need to be examining. But dairy products come up in more instances for various reasons and for various nutrients and so I think we probably have a medley of nutrients that we need to be exploring. In addition there is one article in the scientific literature that suggests that one of the mechanisms of Vitamin D may be as a stimulator of IGF secretion, but that hasn't been followed up at this point in time. (See Jose Manuel Gomez. The Role of Insulin-Like Growth Factor I Components in the Regulation of Vitamin D. (2006) Current Pharmaceutical Biotechnology 7, 125-132.)

One final comment, between the Friday that the prepublication releases went out to the press and the following Tuesday when our paper came out in the Canadian Medical Association Journal on April 25th, over 322 newspapers throughout the world covered this story. And for the next week and a half my telephone and my e-mail were absolutely swamped. I received all sorts of interesting comments from "how dare you promote milk consumption, don't you know it is the banned food," to "thank you for letting us know

that this is a national problem." I am still getting comments. So it is very controversial. But in Canada we are trying to get the message out that we do have a public health issue that we have to deal with in regard to our vitamin D consumption and that was the background for this study.

DISCUSSION:

DR. RICH-EDWARDS: Why is milk not recommended to pregnant and lactating women in Canada?

DR. KOSKI: Generally, it is driven by the lay press, and I will say, again, the five most stated reasons provided by our women were self-reported lactose intolerance, wanting to have lower fat, (they see milk as not being a protein source, they see it as a fat source), their concerns about the development of diabetes in their offspring, and concerns about the development of allergy. So they restrict for all the reasons that have made little inroad into the scientific consensus.

DR. RICH-EDWARDS: Are there actual recommendations from clinical bodies saying don't drink milk?

DR. KOSKI: No, there is no formal recommendation by a clinical body, but if you ask pharmacists, nurses, physicians they will not recommend milk consumption for women, and over 50 percent of the women report being advised not to drink milk by a health professional.

DR. ITO: Assuming that there is a seasonal variation of vitamin D in the maternal blood, did the paper you cite on the relationship between bone density and maternal vitamin D intake discuss whether there's a relationship between bone mass and timing of birth?

DR. KOSKI: Yes. They do make a reference to it. They looked across all seasons, but it is the *in utero* exposure that they emphasize.