

A woman with blonde hair is shown in profile, blowing bubbles. The background is a soft green with many bubbles of various sizes. The text is overlaid on the image.

Look's Who's Talking: Having a Baby when you have MS

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Disclosure

- Consultant – Genzyme, Novartis, Questcor, TEVA Neuroscience



Program Objectives

- 1. Identify fiction versus facts about pregnancy in MS**
- 2. Describe the relationship between pregnancy and MS**
- 3. Identify issues related to DMTs in pregnancy, delivery & breast feeding**
- 4. Describe nursing implications**

Multiple Sclerosis

- **Multiple sclerosis (MS) is an inflammatory disease of the central nervous system**
 - **Mainly affects women**
 - **Onset age 20-40 years**
 - **Caucasians**
 - **~ half million with MS in USA**
- **Relationship between MS & Pregnancy? Planning?**





Pregnancy & MS

- Does pregnancy affect the course of MS?
- Does MS affect the ability to become pregnant and maintain a “normal” pregnancy & delivery?
- We will try to answer these questions...



Fiction VS Facts

- Pregnancy is contraindicated in MS
- MS women can potentially have more issues during their pregnancy
- Bonding is possible only by breastfeeding
- MS women are allowed to have steroids during pregnancy



Fiction VS Facts

- There is no evidence about outcomes of MS women taking DMAs during pregnancy
- Childbirth must be via C-Section & not vaginal delivery
- Based on a Danish study babies of MS women are small for their gestational age
- MS women are not allowed to have epidural



Fiction

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Facts

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Multiple Sclerosis

- No evidence that MS affect:
- Fertility
- Conception
- Fetal viability
- Delivery





Sexual Dysfunction Fertility & Conception

- MS has NO physiological effect on fertility
- Other factors that may affect your ability to conceive:
 - 50-90% of patients with MS have sexual issues
 - Sexual Issues in males & females: Erectile dysfunction, ejaculation dysfunction, Vaginal dryness, decreased libido, difficulty achieving orgasm, numbness
 - Secondary issues: fatigue, weakness, B&B
- Sexual dysfunction may affect rates of conception
- Counseling & treatment/referrals are required for males or females with above related issues

Pregnancy & MS



- MS does not have a detrimental effect on pregnancy
- The incidence of Miscarriages, stillbirth, congenital abnormalities, prematurity, & Complications of pregnancy, such as eclampsia, do not increase in women who have MS
- No need for high risk management unless has history of miscarriages or other problems or twin pregnancies or higher



Factors that may affect women during their pregnancy

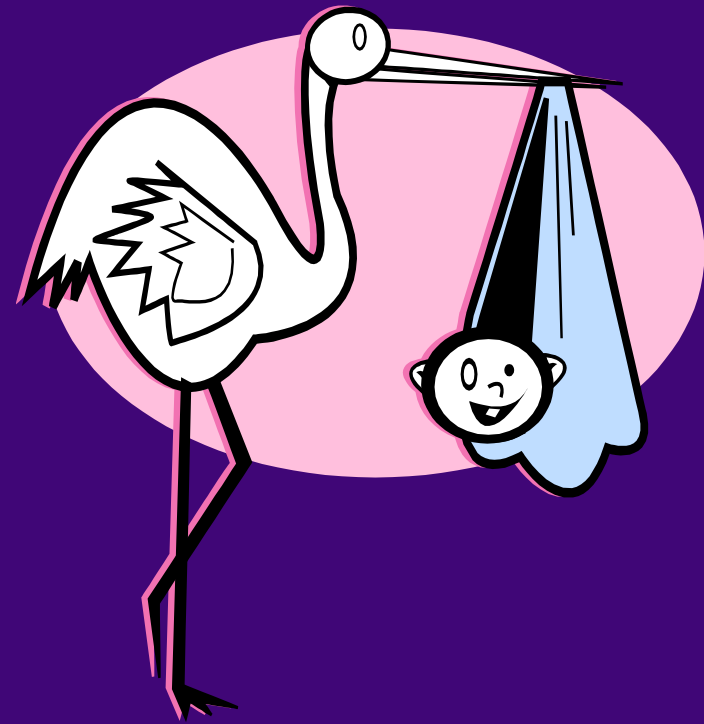
- Bladder & Bowel issues / UTIs*
- Balance & mobility concerns
- Increased risk for falls
- Emotional issues; depression, anxiety
- Increased fatigue
- Decreased endurance
- Lack of support
- Financial concerns

*UTIs = Urinary Tract Infections



Potential Contraindications to Pregnancy

- A progressive disease
- High disability score (EDSS)
- Lack of support system
- Emotional, financial, & care taking support network issues
- Cognitive impairment





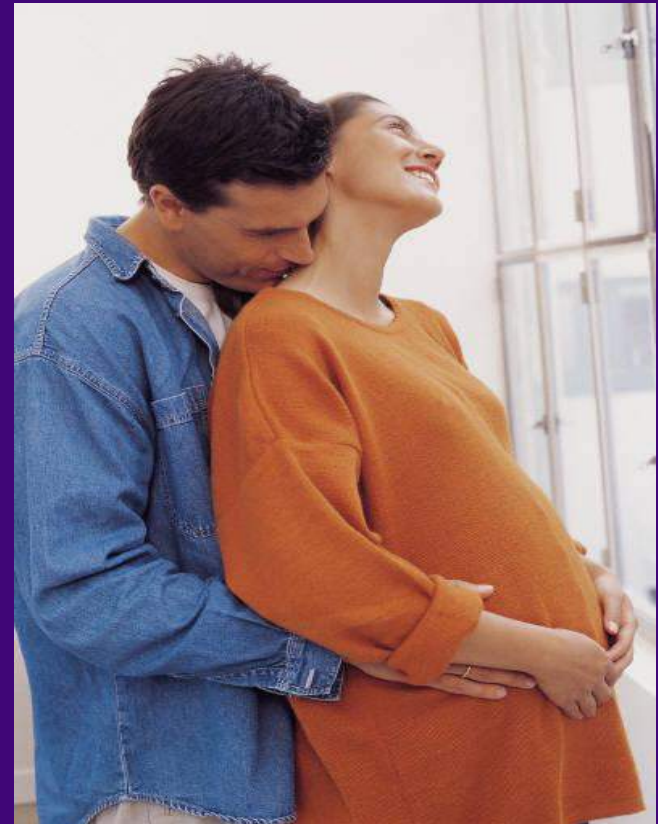
Why Women with MS do better during Pregnancy?

A few potential hypotheses may explain this in the following slides;

However, there is a small percentage of women who relapse during their pregnancy!

Pregnancy & MS

- **Potential Protective Effect by these hormones/mechanisms:**
- **Estrogen**
- **Progesterone**
- **Human Chorionic gonadotropin (HCG)**
- **α Fetoprotein (Pregnancy immuno-regulatory)**
- **Calcitriol (vitamin D)**
- **Pregnancy suppressing Th1 activation**





Hormones & Pregnancy

- Immunomodulatory effects by hormones
- Remember: Risk of thrombosis in women with limited mobility & risk of thrombosis with birth control pills / hormone replacement therapy?
- A pilot study - using pregnancy doses of estriol in 12 non-pregnant MS women
- Patients followed clinically and radiologically for 6 months to establish a baseline level of disease activity before taking any medication
- Then, treated with oral estriol for 6 months, with observation continuing for 6 months after the estriol was discontinued
- Therapy was tolerated well except for menstrual irregularities

Hormones & Pregnancy - cont.

- Trial results
- Decrease in disease activity in RRMS
- Decrease in number and volume of gadolinium enhancing lesions
- A reduction in new lesions formation
- No benefit in SPMS



I'M OUT OF ESTROGEN And I HAVE A GUN





Why women with MS do better during pregnancy?

- Immune system shift during pregnancy
- Natural immunosuppression
- The immune system during pregnancy changes from predominantly cell-mediated (T cell) to predominantly antibody mediated (B cell)
- A balance between cell mediated and antibody mediated immune system changes
- This shift benefits the pregnancy because it allows the presence of the fetus to continue despite its being an allograft with half of its antigens inherited from the father and thus foreign to the mother
- After delivery there is reverting of the immune system to its customary balance between the cell mediated and antibody mediated systems



**The next few slides –
demonstrate the course of
pregnancy in MS women – a
few clinical trials that
show decrease rate of
relapses during pregnancy!**



Pregnancy & MS

- **Pregnancy is a protective period**
- **A study of 227 pregnancies**
- **The frequency of relapses decreases during pregnancy (especially during - third trimester)**
- **The relapse rate increases in the first three months postpartum, as compared with the rate during the year before pregnancy**
- **Confavreaux et al., NEJM 1998; 339, 285-291**



The PRIMS trial

- Prospective multicenter trial - 254 pregnant MS women
- Relapse rate decreased during pregnancy by 70%
- Decrease from a baseline of 0.7 relapse rate per patient per year (year prior to the pregnancy) to a low 0.2 per patient per year
- PRIMS large prospective study
- Vukusic et al., Brain, 2004; 127, 1353-1360





**Long Term Effects of
Pregnancy – the effect
number of pregnancies on
the course of MS – a few
trials in the next few slides!**



Effects of pregnancy

- ? effect on long term progression of MS
- ? effect of pregnancy on long term course of disease
- Parity does not affect MS onset
- Parity has some effect on progression of disease
- Decision RE pregnancy – individual decision based on lifestyle/resources, disability and disease course



MS & Pregnancy

- Prognosis & Pregnancy
- A small study compared the progression in 7 childless MS women, 10 women who developed MS at least 6 months after pregnancy & 12 women who developed MS before or during pregnancy
- Progression was greatest in the childless women & lowest in the women with onset after delivery
- The risk of transition into a progressive course was 3.2 times higher in the never-pregnant group than in the post-pregnancy group
- **Stenager et al. Acta neurologia Scand, 1994, 90, 305-308**
- **Runmarker & Andersen. Brain 1995, 118, 253-261**





- Length of pregnancy in MS & Delivery types in MS based on a Danish Registry Data - 1967-2002; Next few slides:
 - Increased number of assisted delivery & C-section in women with MS
 - Apgar scores, perinatal mortality, & birth defects did not differ between MS & control groups
 - Low birth weight among babies for mothers with MS

Delivery & Birth outcome

- Medical British Registry of Norway 1967-2002
- 461 MS mothers with 649 births
- Control 1,029,456 mothers with 2,102,430 births
- Dahl et al. Neurology 65, 1961-1963



Pregnancy & Outcome



- Characteristics of neonates

	MS	Control
• Preterm	7.9	6.2%
• Mean birth weight	3,268g	3,391g
• Low birth weight	4.9	5.2%
• High birth weight	2.3	3.5%
• Small for gestation	13.5	11.3%

•Dahl et al. Neurology 65, 1961-1963



Delivery Outcomes

- Total operative deliveries (forceps, vacuum, & Cesarean section)

	MS	Control
• 1967-1980	12.9%	8.6%
• 1981-1990	32.6	18.6
• 1991-2002	26.4	20.6
• Forceps & Vacuum		
• 1967-1980	3.2	4.7
• 1981-1990	15.3	7.4
• 1991-2002	7.9	7.6

Dahl et al. Neurology 65, 1961-1963



Delivery Outcomes

- Cesarean delivery
- | | MS | Control |
|-------------|------|---------|
| • 1967-1980 | 9.7 | 3.9 |
| • 1981-1990 | 17.4 | 11.3 |
| • 1991-2002 | 18.5 | 13.2 |
- Apgar scores, perinatal mortality, & birth defects did not differ between MS & control groups
- NMSS after discussions with OB-GYNs – No major concerns related to results of this registry outcomes

Dahl et al. Neurology 65, 1961-1963



MS Babies

- based on the registry
- Increased rate of small neonates for their gestational age
- Reduced mean birth weight & length but a normal head circumference



Dahl et al. Neurology 65, 1961-1963



Low birth possible etiology

- Other comorbidities
- Insufficient nutrition
- Bowel, bladder, sexual dysfunctions which may affect the baby development
- Increased rate of UTIs & increased need for induction of labor
- Alterations in uterine function related to neuronal dysfunction could produce suboptimal intrauterine environment & influence fetal growth





In Contrast - No effect on birth weight; Worthington, 1994

- A 3 year prospective study
- Normal distribution of weight & head circumference in babies born to mothers with MS
- No reported evidence that children of mothers with MS are physically or mentally disadvantaged
- Worthington J. J of Neurology 241, 228-233, 1994



- MS treatment During pregnancy –
Next Few Slides:
- Majority of clinicians discontinue the disease modifying agents (DMAs) pre conception & during pregnancy
- Steroids during pregnancy – question of safety & timing of steroids along the 3 trimesters
- Paying attention to category of medications and discussions with OB-GYN



Treatment During Pregnancy

- The FDA & NMSS – DMAs should not be used by women who are trying to get pregnant, are pregnant, or breastfeeding
- Time stopping DMA prior to conceiving
- Lack of knowledge
- Lack of evidence about effects of these medications on the fetus





IV steroids during pregnancy

- Steroids may be given when indicated for -
Acute major relapses
- Risks of intravenous steroids during 1st & 2nd trimesters but less during 3rd trimester
 - Intrauterine growth retardation
 - Premature rupture of the membranes
 - Worsening of pregnancy induced maternal complications i.e. HTN, gestational diabetes, osteoporosis



Steroids during each Trimester

- Steroids should be avoided in the first trimester due to organogenesis (see previous slide)
- Steroids may be given in the second trimester but with caution (see previous slide)
- OB-GYN approve steroids treatment during the 3rd trimester only if needed – help mature the fetus lungs



Pregnancy Categories

- Category A – A proven absence of fetal risk
- Category B – No known adverse effects on fetal development in animals
 - Glatiramer Acetate (Copaxone®)
- Category C – Known fetal risk in animals
 - Interferon- β (Avonex, Rebif, Betaseron), Fingolimod (Gilenya), Natalizumab (Tysabri)
- Category D – Documented human fetal risk
 - Mitoxantrone (Novantrone) & other chemo drugs
- Category X – high fetal risk – Teriflunomide (Aubagio)



Pregnancy & Glatiramer Acetate (GA)

- 562 pregnancies in women with MS while D/C GA during the first trimester (post-marketing)
- 72% healthy live births
- 20% spontaneous abortions
- 3% elective abortions
- 2.7% congenital abnormalities (2 cases of down's syndrome, 2 cases of failure to thrive, single cases of finger anomaly, lung malformation, CVA, cardiomyopathy, congenital short femur, urethrostenosis, Brain & skull abnormality in pt on Avonex for 18 weeks & Copaxone for 21 weeks)
- 1% ectopic pregnancies
- 0.5% still births
- Similar results as in the general population



Pregnancy Registry by company

Pregnancy & Interferon

- Small sample of women that got pregnant while on interferon & stopped
- 26% Spontaneous abortions
- 15-20% in the general population
- 3.2% fetal death
- 0.7% in the general population
- Adherence to the recommendation of stopping interferon prior to conceiving



Pregnancy Registry by company

Mitoxantrone (Novantrone)



- Animal studies
- Premature birth
- Low birth weight
- Abnormal renal development
- Infertility in women

Note: Next update – will try to include registry for Natalizumab & Fingolimod & Teriflunomide



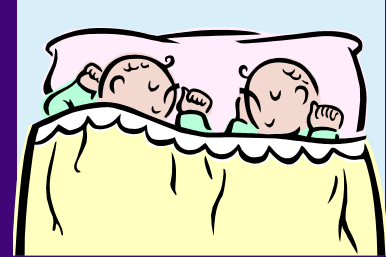
Next Few Slides:
Postpartum period in
women with MS & the risk
of Relapses;
IV Immunoglobulin
postpartum;
Breastfeeding in MS;

Postpartum & MS

- Increased Relapse rate during the first trimester postpartum
- Initiation of DMA
- Breastfeeding timing



MS after Pregnancy



- PRIMS Trial
- The relapse rate in the first 3 postpartum months increased to 1.2 per patient per year
- 70% increase in RR above baseline
- 20-40% of women will experience a relapse during the first 3 months postpartum
- 167 women followed for 2 years after delivery;
- The relapse rate similar to the pre-pregnancy year (Vukusic et al.)



Postpartum IVIG

- Two studies have shown positive effect of the use of intravenous immunoglobulins (IVIg) postpartum
- The IVIg reduced the number of relapses postpartum & was safe
- The mechanism by which the IVIg acts on relapses is unknown, but is likely related to its inhibition effect on the immune system
- Further studies are needed to better understand the effects of IVIg during the postpartum period
- (Achiron et al., 1996, and Orvieto et al., 1998)

Breastfeeding & MS

- It is unknown whether breastfeeding alters the risk of relapse rate
- There are very few studies about the effects of breastfeeding on disease activity
- The available data do not indicate a negative impact





Breastfeeding in MS

- Breastfeeding is permitted for a few weeks or months after delivery
- The decision to breastfeed is based on each patient's condition and their health and MS status during the pregnancy and prior to the pregnancy
- There should be a discussion between the parents or partners with their MS team about the feasibility and safety of the decision to breastfeed and forgo initiating a disease modifying agent immediately after giving birth



Breastfeeding Study

- Langer-Gould et al. has followed 32 pregnant women with MS and 29 matched age pregnant controls
- The prospective study showed that 87% of women with MS who did not breastfeed or began regular supplemental feedings within 2 months postpartum, had postpartum relapses compared with 36% women with MS who breastfed exclusively at least for 2 months (87% vs. 36%)
- The study suggests that exclusive breastfeeding and suppression of menses significantly reduce the risk of postpartum relapses in MS (Langer-Gould et al., 2009)
- Larger studies are needed to confirm these results



Other factors that may affect Pregnancy in MS

- Medical issues
- Bladder issues
- Bowel
- Mobility
- Fatigue
- Secondary issues
 - Urinary tract infections
 - Skin issues / sores
- Social issues
- Ability of the couple to care for their infant / other children
- Financial issues / insurance
- Emotional issues
- Post-partum depression / Anxiety





Clinical implications

- **Pregnancy is not contraindicated for most women with MS**
- **Parenthood & relationship: Mother or father with MS to have discussions about planning pregnancy with the MS team**
- **It is not recommended to be on any of the DMAs during pregnancy or while breastfeeding**
- **There is no clear understanding of the effects of breastfeeding on relapse rate in MS**
- **A recommendation for women that had relapses during their pregnancy to - Initiate DMAs & forgo breastfeeding**
- **A thorough discussion about postpartum options between the mother & partner and the MS team need to take place on an ongoing basis**
- **The care should be individualized based on the severity of disease & course of illness**



Implications for nurses

- **Mastering the available data about women issues in multiple sclerosis**
- **Counseling about pregnancy, delivery and caring for the child and their relations with MS**
- **Counseling RE all aspects of pregnancy**
- **Educating patients & family members**
- **Encourage nurses/peers to do more research in this area**
- **Investigate further the relationship between women issues and multiple sclerosis**



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form and provide feedback
to enable me to improve
the program and update it
as necessary!**