

The effect of disease modifying therapies for MS on fertility and pregnancy

Mentors:

Dr. Eldad Katorza

Dr. Gili Givaty

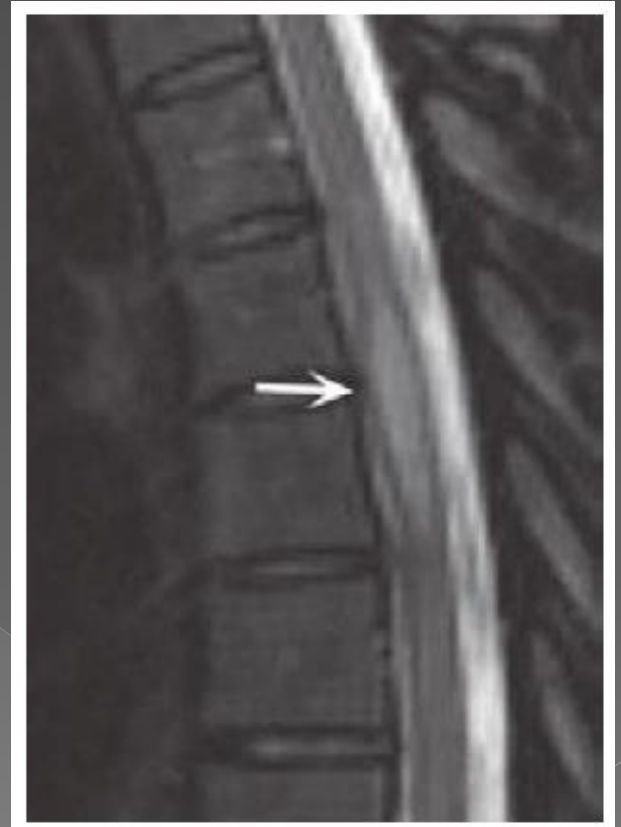
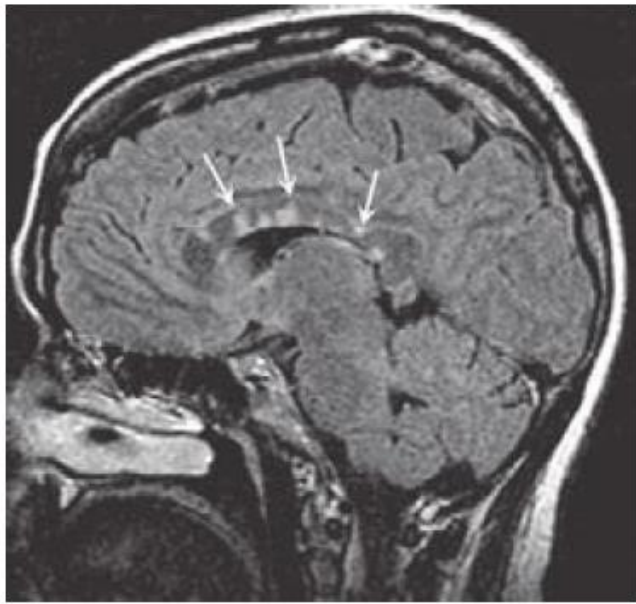
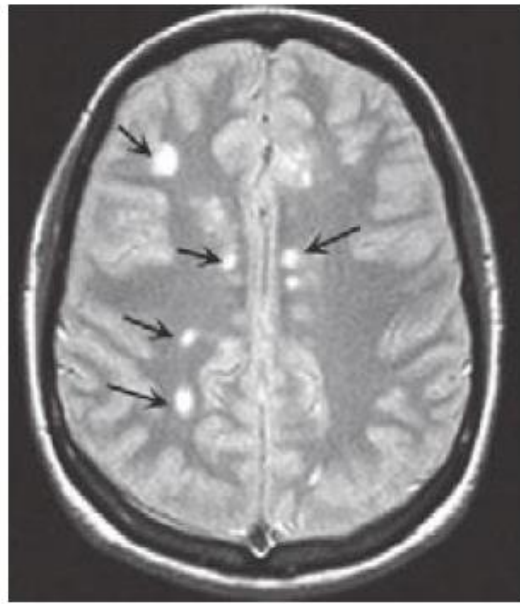
Student:

Keshet Pardo

Multiple Sclerosis (MS)

- ◉ Autoimmune disease of the central nervous system
- ◉ Chronic inflammation
- ◉ Demyelination
- ◉ Gliosis
- ◉ Neural loss

MS - MRI

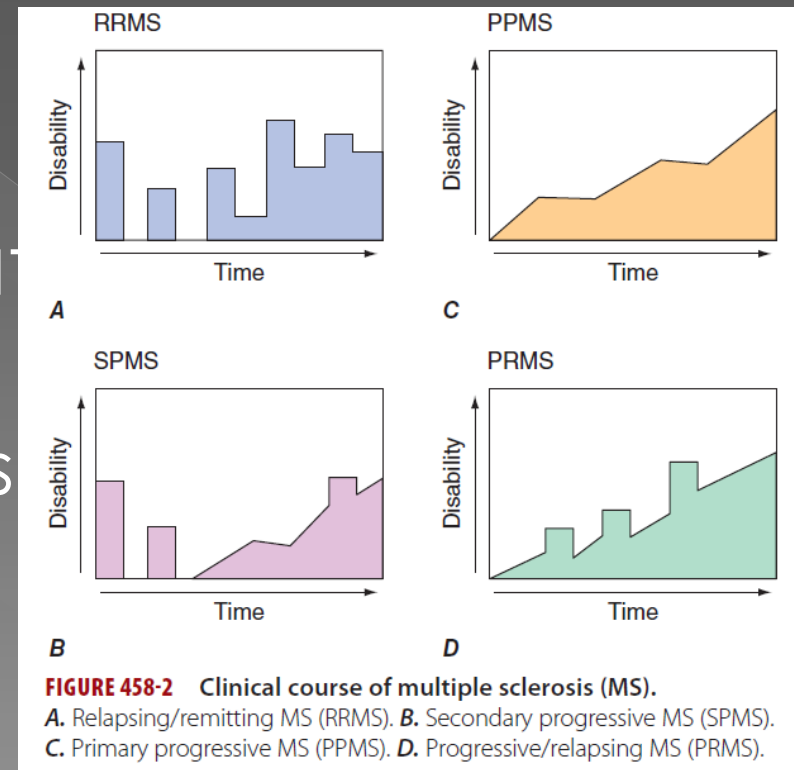


MS - Epidemiology

- 350,000 patient in the US
- 2.5 millions patients worldwide
- 3:1 more common in women
- Age of onset between 20-40
- Israel – around 5,000 patient with MS

MS – Disease course

- **Relapsing-remitting MS (RRMS)** – 85% of the patients
- **Secondary Progressive MS (SPMS)** – for patients with RRMS the risk for developing SPMS is 2% each year.
- **Primary Progressive MS (PPMS)** – 15% of the patients
- **Progressive/Relapsing MS (PRMS)** – 5% of the patients



MS - Clinical manifestation

- ◉ Weakness of the limbs
- ◉ Spasticity
- ◉ Optic neuritis
- ◉ Diplopia
- ◉ Sensory symptoms
- ◉ Ataxia
- ◉ Bladder dysfunction
- ◉ Constipation
- ◉ Cognitive dysfunction
- ◉ Depression
- ◉ Fatigue
- ◉ Sexual dysfunction
- ◉ Vertigo

Treatments for MS

- Treatment of acute attacks (exacerbations)
 - > Glucocorticoids
- Disease modifying therapies
 - > INF β
 - > Glatiramer Acetate
 - > Natalizumab
 - > Fingolimob
 - > Dimethyl Fumarate
 - > Teriflunomide
 - > Mitoxantrone
 - > Alemtuzumab

MS and Pregnancy

- ◉ Reduction in relapse frequency during pregnancy (especially in the final trimester).
- ◉ Increase in relapse risk in the first 3 months postpartum.
- ◉ Some studies showed lower birth weight in babies born to MS patients

The effect of DMTs on pregnancy outcomes

- ◉ DMT is usually discontinued during the pregnancy and breast feeding → limited information
- ◉ Teratogenic effect:
 - Fingolimod, Mitoxantrome, Teriflunomide
- ◉ INF β – lower birth weight, preterm birth
- ◉ Glatiramer Acetate – not associated with any risk

Houtchens,, Multiple sclerosis and pregnancy: therapeutic considerations. J Neurol, 2013.
Amato, M.P, Fertility, pregnancy and childbirth in patients with multiple sclerosis: impact of disease-modifying drugs. CNS Drugs, 2015.

The effect of DMTs on Fertility

- ◉ Drugs that show no effect:
 - > INF β , Glatiramer Acetate, Fingolimod, Teriflunomide
- ◉ Natalizumab – reduced fertility in animals (no information in humans)
- ◉ Mitoxantrome – amenorrhoea and azoospermia

The dilemma

- Should newly diagnose MS patient that are interesting in having kids should hold off treatment till after the pregnancy?



Our study



Methods

- Comparison between two groups:

RRMS Patients without
pre- conception
treatment

RRMS Patients with
pre- conception
treatment

Methods

- Multivariate analysis adjusted to age, disease severity, known fertility problems and previous pregnancy
- The information regarding the patients will be taken from Sheba MS Center's data base

Parameters for comparison

- ◉ Time to conception
- ◉ Need for medical or artificial intervention
- ◉ Pregnancy loss, fetal anomalies
- ◉ Gestational week delivery, birth weight, mode of delivery, Apgar score
- ◉ Rate and number of relapses and disease progression after the pregnancy

