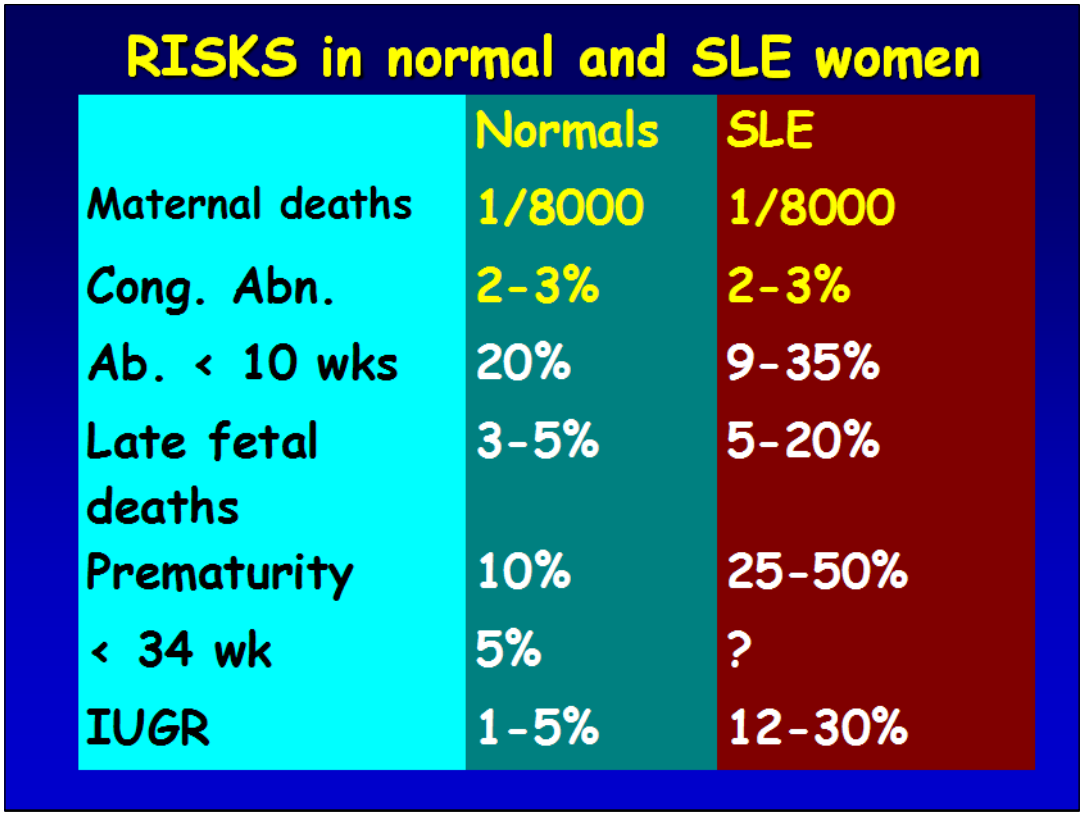
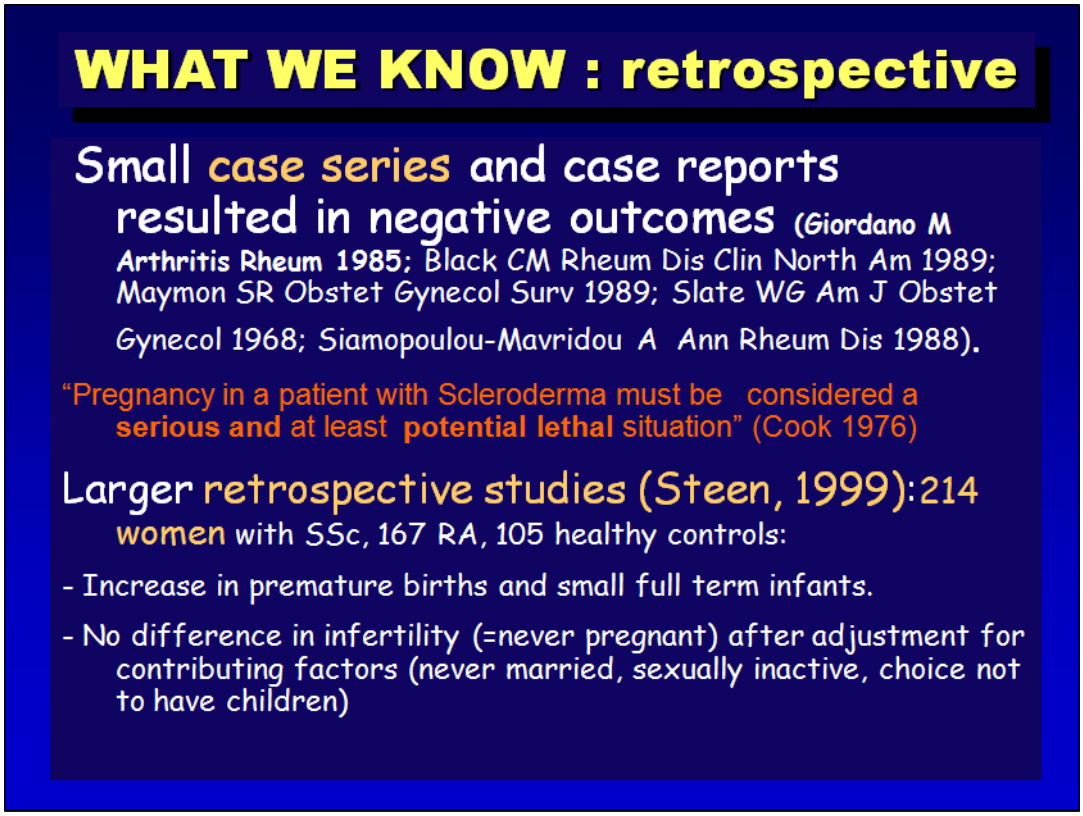



Normal pregnanciesL SLE; and Scleroderma?




With the mean age of onset of scleroderma symptoms in the early 40s, almost half of the women with this illness have the potential of becoming pregnant after the onset of their illness. Years ago, most women would have completed their pregnancies prior to this age, but more recently, women are frequently delaying pregnancy. Thus, there is an increased likelihood for a concurrent pregnancy in women who develop scleroderma early in their adult life.

## WHAT WE KNOW: prospective

Steen, Obstet Gynecol 1999.

- 59 women, 91 pregnancies over 10 years.
- Questionnaire based.
- No increase in miscarriages, except in long standing diffuse scleroderma
- Prematurity: 29% (all but one infants survived)
- Raynaud improved
- Esophageal reflux worsened
- 3 renal crisis, in early diffuse scleroderma

# Large administrative database:

- Chakravarty et al. Obstet Gynecol, 2008 (**not possible to identify single patients**):
- SSc was associated with an increased risk of:
- - hypertensive disorders including preeclampsia (OR 3.71,),
- - IUGR (OR 3.74, 95%CI 1.51–9.28),
- - increased length of hospital stay.


So we had studies from 1999, questionaire based or from large administrative database, and the argument was somehow neglected in the pregnancy meetings. Italian pts asked us some more answers

# WOMEN

- *Data prospectively* collected one year before pregnancy, during each trimester and after delivery were *retrospectively* analysed.
- 25 Italian centers prospectively followed 109 pregnancies in 99 women from 2000 to 2010
- Mean age at conception: 31.8 yrs
- Duration of disease at conception: 60 months (2-193)
- 102 ACR criteria, 54 limited (lSSc) and 48 diffuse (dSSc) cutaneous SSc;
- 6 early SSc.

| | SSc | GOP | SLE |
|---|---|---|---|
| N.pregnancies | 109 | 3939 | 147 |
| Pregnancy loss (<10 wk) | 6% (4%) | 8% (5%) | 15% (9%) |
| Prematurity (<34wk) | 25% (10% P<0,01 | 12% (5%) | 17% (2%) |
| Mean gest Age | 36 wk | 38 wk | 38 wk |
| Mean maternal age | 31.8 yrs | 30.9 yrs | 30 yrs |
| Cesarean sections | 52% P<0,01 | 31% | 50% |

Prematurity is the first recognized cause of neonatal mortality and long-term neurological impairments in children.

| | SSc (109 pregn) | GOP (3939 pregn) | SLE (147 pregn) |
|---|---|---|---|
| IUGR | 6% P=0.001 | 1% | 1% |
| Preeclampsia/ hypertension | 2% | 4% | 7% |
| Renal crisis | 1% after delivery | - | |
| Therapeutical abortions | 4% | nd | 1% |
| Very low birth weight < 1500 g | 5% P=0,002 | 1% | Nd |
| SGA | 11% | 10% | 9% |

Hazard Ratios for prematurity in SSc women in IMPRESS study in the Cox Proportional Hazards Model.

| Risk Factor | Hazard ratio | 95% CI | p |
|---|---|---|---|
| Anti Scl70 | 0.26 | 0.08-0.85 | 0.013 |
| Folic acid | 0.30 | 0.10-0.91 | 0.026 |
| Corticosteroids | 3.63 | 1.12-11.78 | 0.048 |

In multivariable analysis (including IUGR, very low birth weight, aSCL-70, corticosteroids, folic acid), only corticosteroids were associated with preterm deliveries , while folic acid was protective and so were aSCL-70 antibodies

- Diffuse vs Limited cutaneous:

**NO SIGNIFICANT DIFFERENCE IN PREGNANCY OUTCOMES**

# SEVERITY OF DISEASE?

## >3 Medsger disease severity scale

No patient had pulmonary hypertension (PAH) (mean PAP>25mmHg), severe renal or cardiac involvement at baseline

2 women had a severe gastrointestinal disease: 1 IUGR and preterm CS

3 women had severe lung fibrosis: no obstetrical complication.

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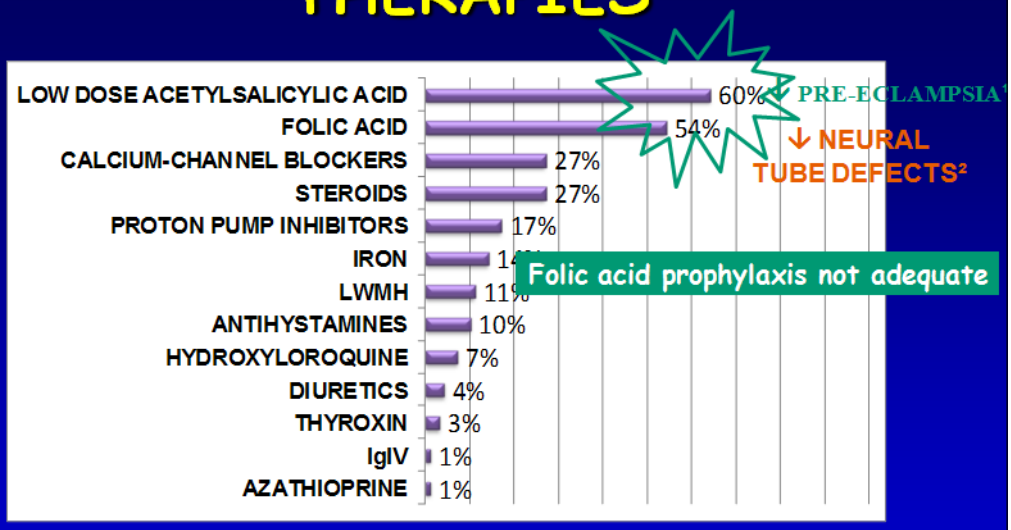
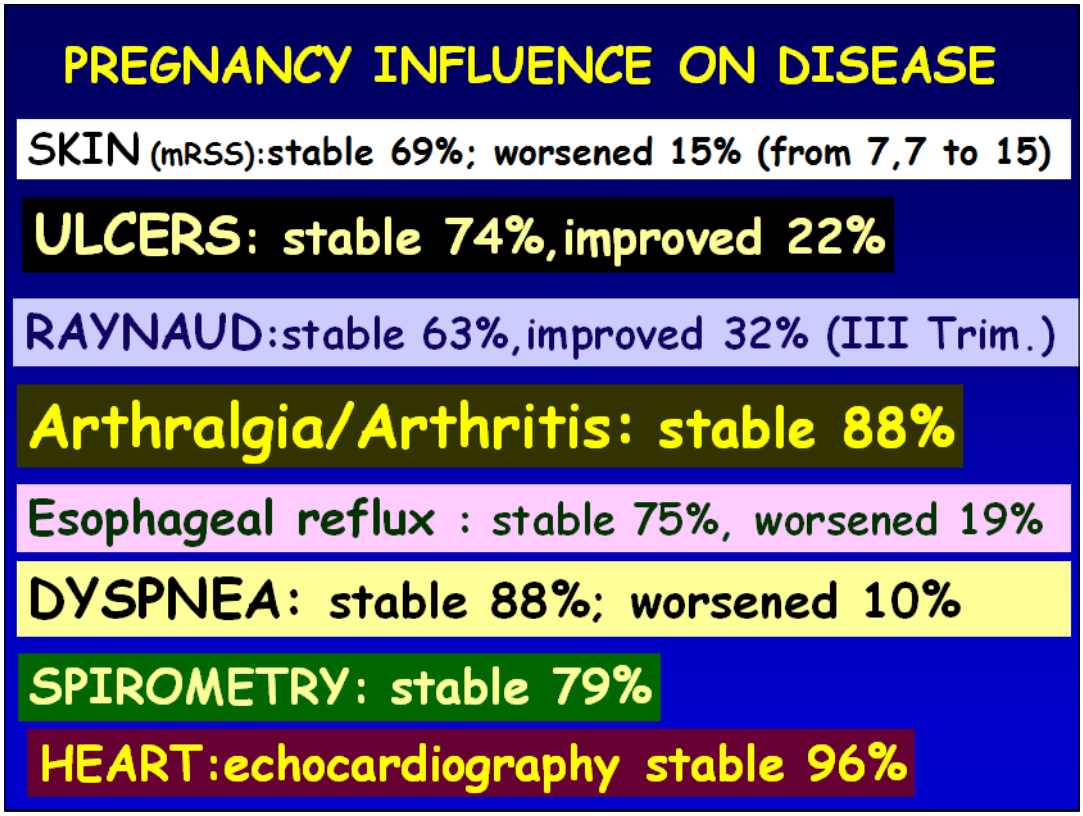
# THERAPIES

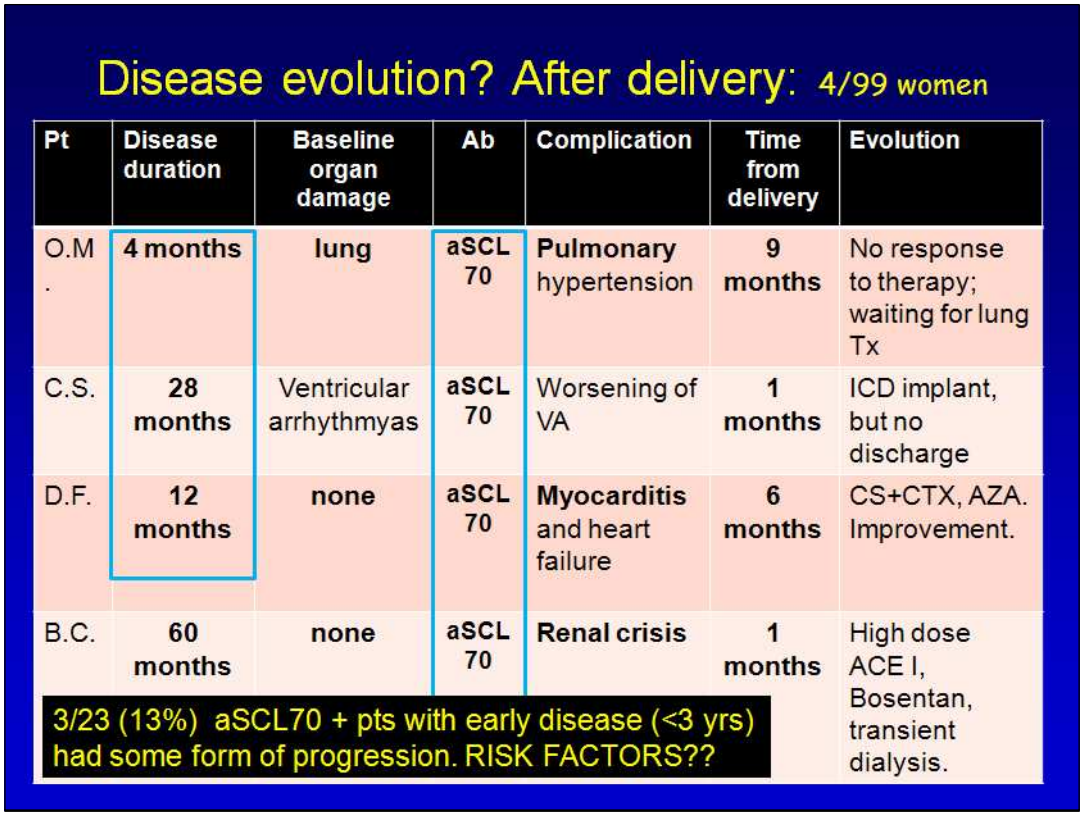



[1] *Bujold E et al.* Acetylsalicylic acid for the prevention of preeclampsia and intra-uterine growth restriction in women with abnormal uterine artery Doppler: a systematic review and meta-analysis. J Obstet Gynaecol Can 2009 ; 31(9): 818-26.

[2] *Wolff T et al.* Folic acid supplementation for the prevention of neural tube defects: an update of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2009; 150(9): 632-9.




The disease remained stable during pregnancy and in the subsequent year in most SSc patients (Table 3), but there were some noteworthy changes. In 15% (17 patients: 12 dcSSc, 4 lcSSc 4, 1 early) the mRSS was significantly worse after pregnancy, rising from a mean of 7.7 to 15. Raynaud's phenomenon temporarily improved (32%) from the second trimester and a similar improvement was observed for digital ulcers (22%); these benefits were lost after delivery. Dyspnea temporally worsened during pregnancy in 10% of women (two with lung involvement), but none had any organic pulmonary progression. Assisted fecundation procedures were not related to any disease progression.




In all, 13% (3/23) of aSCL-70 positive patients with disease lasting less than three years had some form of progression after delivery.

# IMPRESS: CONCLUSIONS

- Total pregnancy loss low (6%)
- Prematuruty high (25%): CS risk factor, while Folic acid and aSCL70 protective
- Folic acid (Czeizel: Possible association of folic acid supplementation during pregnancy with reduction of preterm birth: a population-based study. Eur J Obstet Gynecol Reprod Biol 2010)
- Increase in IUGR and very low birth weight (<1500 g)
- = SIMILAR to SLE, APS, etc.

- Mild improvement in Raynaud
- Mild worsening of G.I. symptoms
- Progression of the disease during or after pregnancy is rare but possible

avoid pregnancy in cases of severe organ damage and postpone it in cases of early SSc. Remember folic acid and low-dose ASA

Following the above listed reccomandations these women too may experience a natural but extraordinary event: to have a child.

# Pre-conceptional counselling

- Assessment of organ damage; PAH absolute contraindication
- length of disease (>3 yrs),
- Therapy (MTX, MMF); restrict use of CS
- Folic acid supplementation !
- antibodies: anti-toposomerase and anti RNA Polymerase III more aggressive disease, but anti-centromere and rare Abs might be a risk for prematurity. aPL

# During pregnancy

- High-risk obstetric care, including neonatologists
- Cautious use of proton pump inhibitors, anti H1 or Ca+ channel blockers; low dose aspirin; folic acid.
- Avoidance of corticosteroids as much as possible
- Monitoring of fetal growth, uterine and umbilical arteries flows
- Frequent blood pressure monitoring, aggressive treatment of any hypertension (preeclampsia or other)
- Close observation and treatment for premature labor (avoid beta-adrenergic agonists)

# Labor and puerperium

- Epidural anesthesia is preferred
- Special warming of delivery room, intravenous fluids, patients themselves (e.g., extra blankets, thermal socks, gloves)
- Venous access before delivery
- Careful attention to the episiotomy and cesarean section incisions, which generally heal without difficulty
- Continued monitoring postpartum, with early reinstitution of medication and aggressive treatment of hypertension if it is present (don't assume it will resolve following delivery)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Scorza,Tani,Taraborelli,
Tincani, Trotta,Valentini,Valesini,Vanoli,
Vigone,Zeni,Zingarelli


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M. Østensen


After fisnishing IMPRESS 1, we now have a dream: IMPRESS 2, hping useful for pts and tehur family and that women will be happy to b enrollsed in this study