

The Thin-Fat Indian

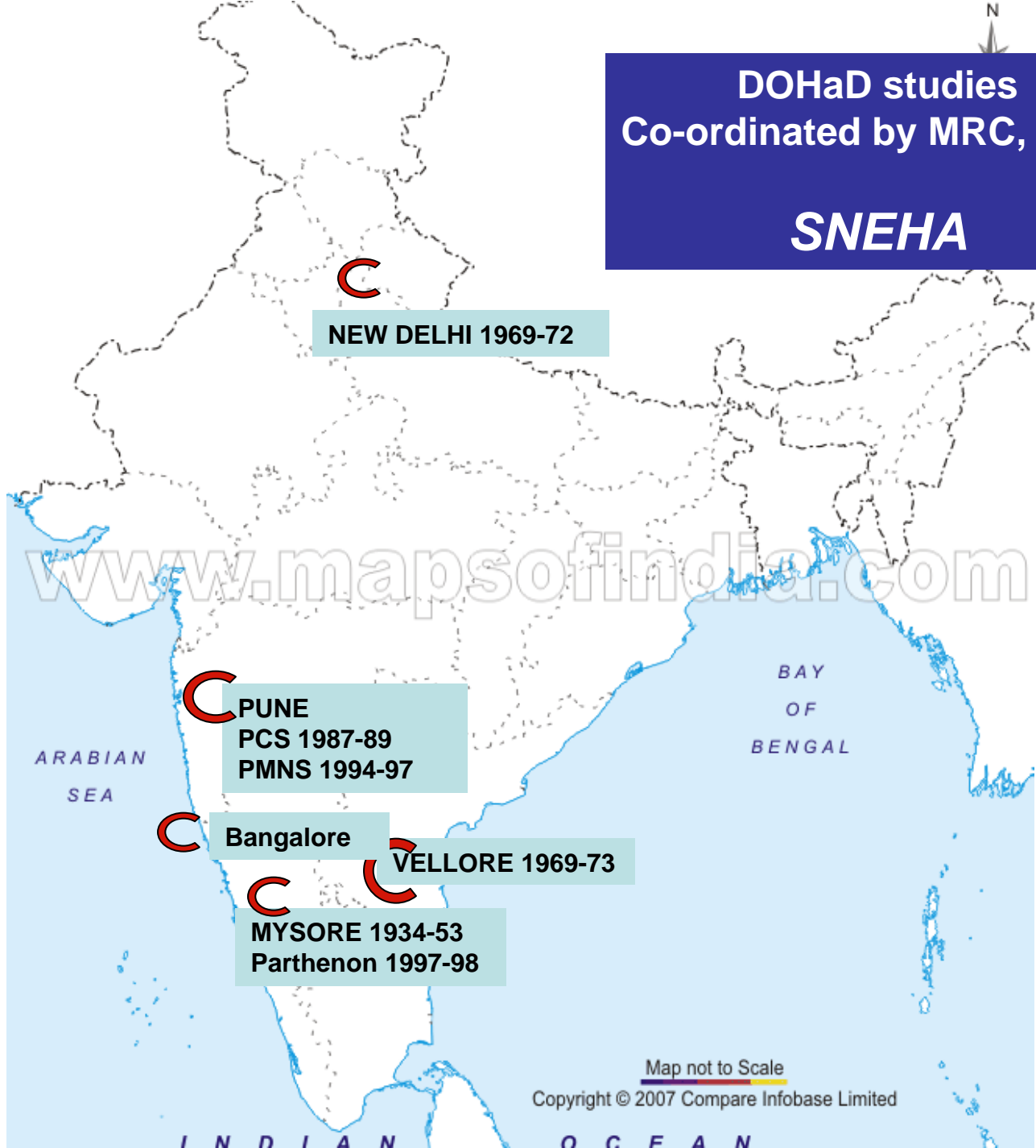


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SNEHA



DOHaD studies
Co-ordinated by MRC, S'ton

SNEHA



NEW DELHI 1969-72

PUNE
PCS 1987-89
PMNS 1994-97

Bangalore

VELLORE 1969-73

MYSORE 1934-53
Parthenon 1997-98

www.mapsofindia.com

Map not to Scale

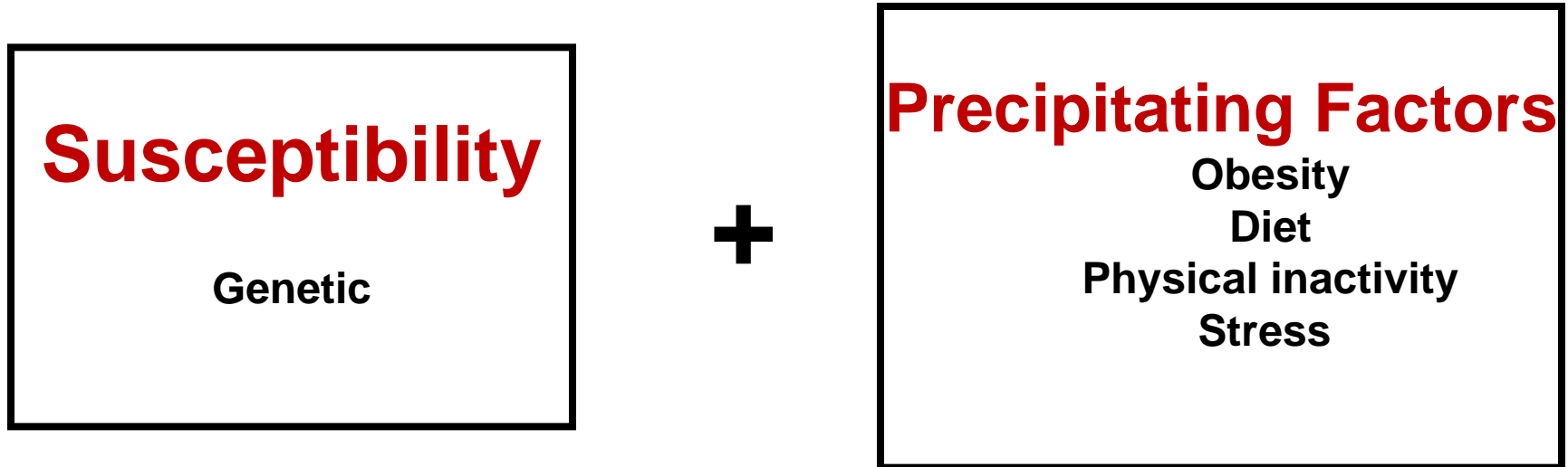
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Nutrition and Diabetes

- ▣ The evidence that malnutrition protects adult populations from diabetes seems unassailable (WHO 1965, TRS 310)
- ▣ Malnutrition is probably a major determinant of diabetes (WHO 1980, TRS 646)
 - A 'new' class of diabetes (IDDM, NIDDM, MRDM)
 - ▣ MRDM (Malnutrition Related Diabetes)
 - PDPD
 - FCPD
- ▣ MMDM (Malnutrition Modulated Diabetes), Cuttack 1996
 - The clinical syndrome may mask underlying form of diabetes, .. *Over a template of IDDM, NIDDM (Rao, Yajnik 1996)*
- ▣ WHO-IDF 1999 classification: MRDM withdrawn !

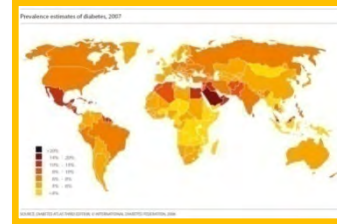
Type 2 Diabetes

The Dogma



- Prevention Trials are based on a gene + obesity model
- Post-reproductive, obese, glucose intolerant
- Food restriction in the end-stage

Diabetes Epidemic: India (a land of paradoxes)



➤ 1907: Diabetes:

What gout is to the aristocracy in Britain (Bose, Kolkata)

➤ 2007: Double Burden

✓ *World's Capital of Diabetes (80 million 2030)*

✓ *Co-existent poverty & undernutrition*

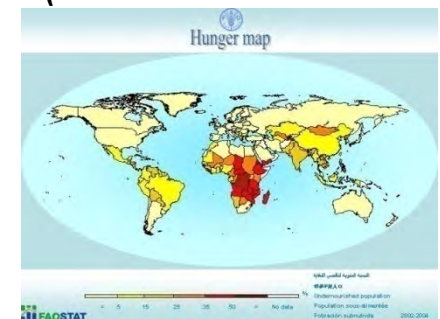
▪ *¼ th population below poverty line (< 1 \$US / day)*

▪ *1/3 rd babies are LBW, 80 million <5y undernourished*

▪ *increasing prevalence of obesity in adults and children (~25% urban affluent)*

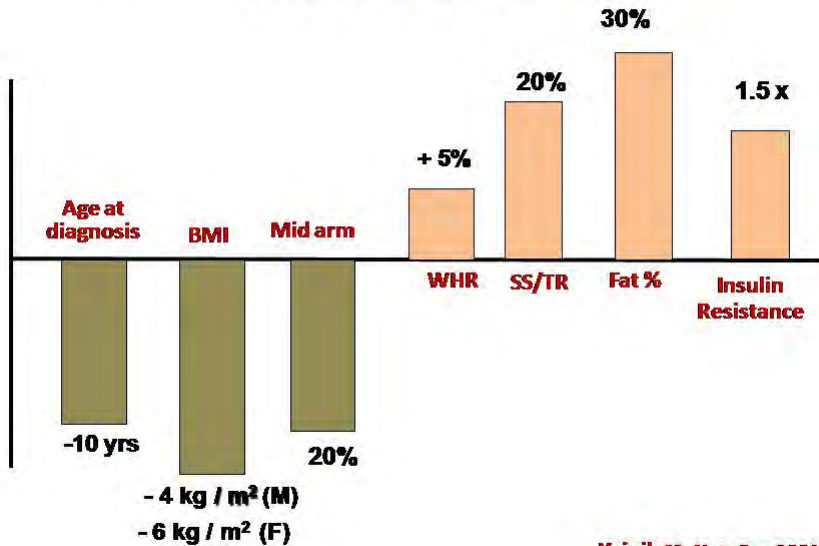
➤ Urban > Rural

➤ Young and the poor



Thin-fat Indian

Newly diagnosed Type 2 DM (Indian vs UK white)

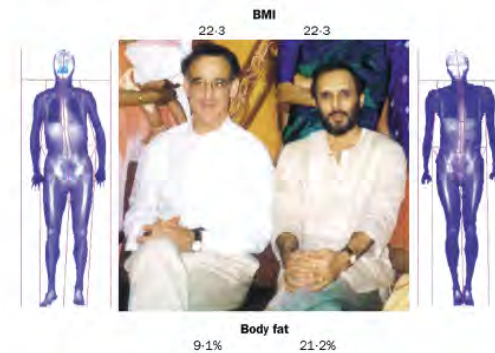


Yajnik CS, Nutr Rev 2001

Clinical picture

The Y-Y paradox

Chittaranjan S Yajnik, John S Yudkin



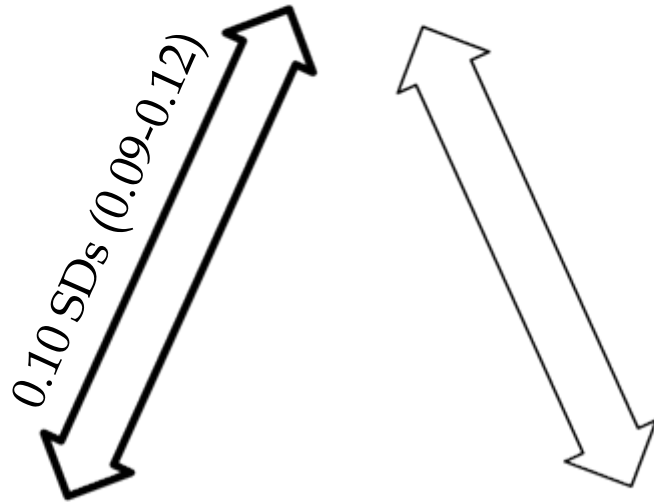
The two authors share a near identical body-mass index (BMI), but as dual X-ray absorptiometry imagery shows that is where the similarity ends. The first author (figure, right) has substantially more body fat than the second author (figure, left). Lifestyle may be relevant: the second author runs marathons whereas the first author's main exercise is running to beat the closing doors of the

elevator in the hospital every morning. The contribution of genes to such adiposity is yet to be determined, although the possible relevance of intrauterine under-nutrition is supported by the first author's low birthweight. The image is a useful reminder of the limitations of BMI as a measure of adiposity across populations.

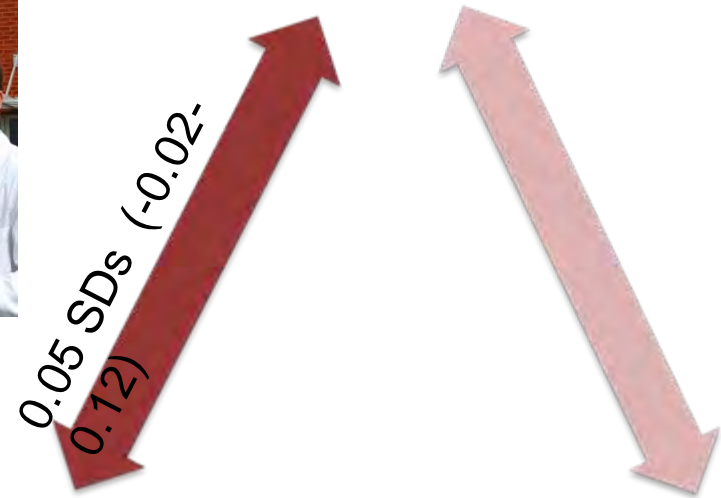
Diabetes Unit, KEM Hospital Research Centre, Rasta Peth, Pune 411011, India (C S Yajnik MD); International Health and Medical Education Centre, University College London, UK (J S Yudkin FRCP)

FTO, Obesity and T2DM

Europeans



Indians



OR 1.27 (1.26-1.37)
Adj. BMI OR 1.03 (0.96-1.10)

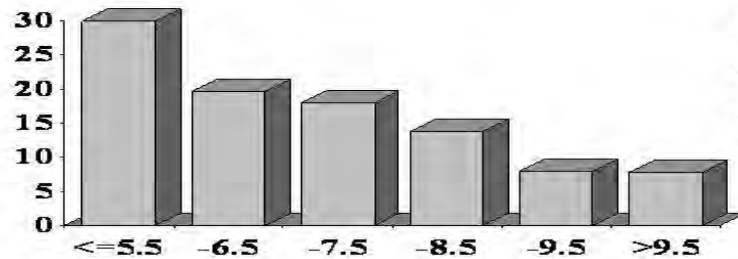


OR 1.26 (1.13-1.40)
Adj. BMI OR 1.21 (1.06-1.37)

Hertfordshire, UK

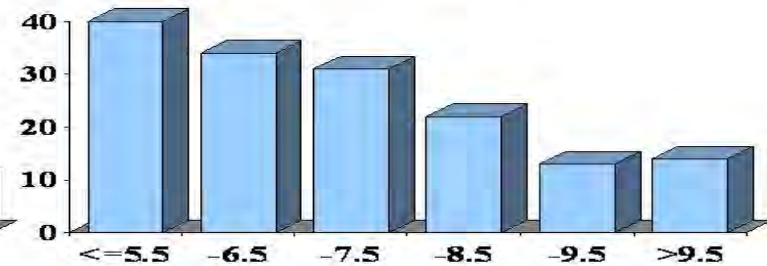
Men aged 59-70 yrs
(n=408)

SYNDROME X



Men aged 64 yrs
(n=370)

IGT + DM



Birthweight (lbs)

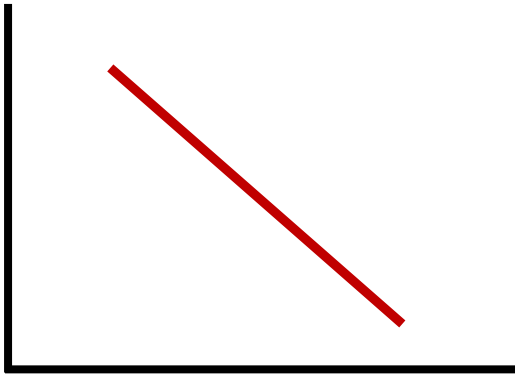
* $p < 0.05$

Hales CN et al, BMJ, 1991

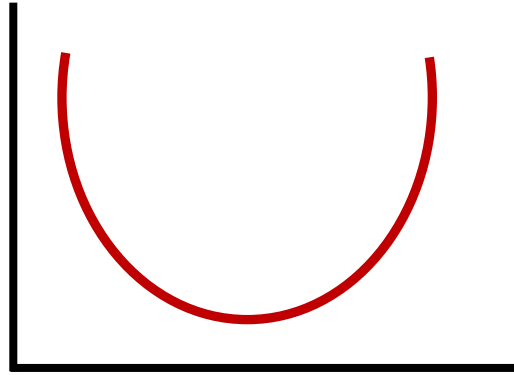
- Continuous, graded
- No LBW threshold
- 1930's, maternal diabetes rare, viable pregnancy unlikely

- **BW is not the exposure, only a marker of adverse intra-uterine exposure**

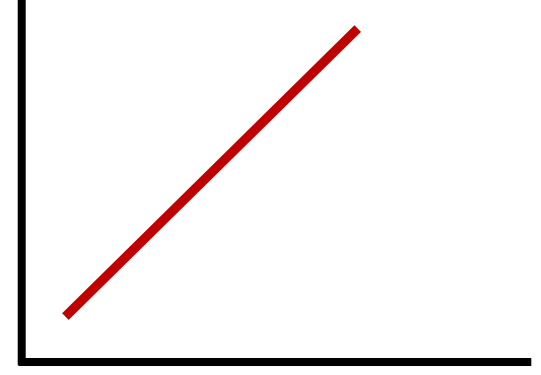
Birth weight and Type 2 DM



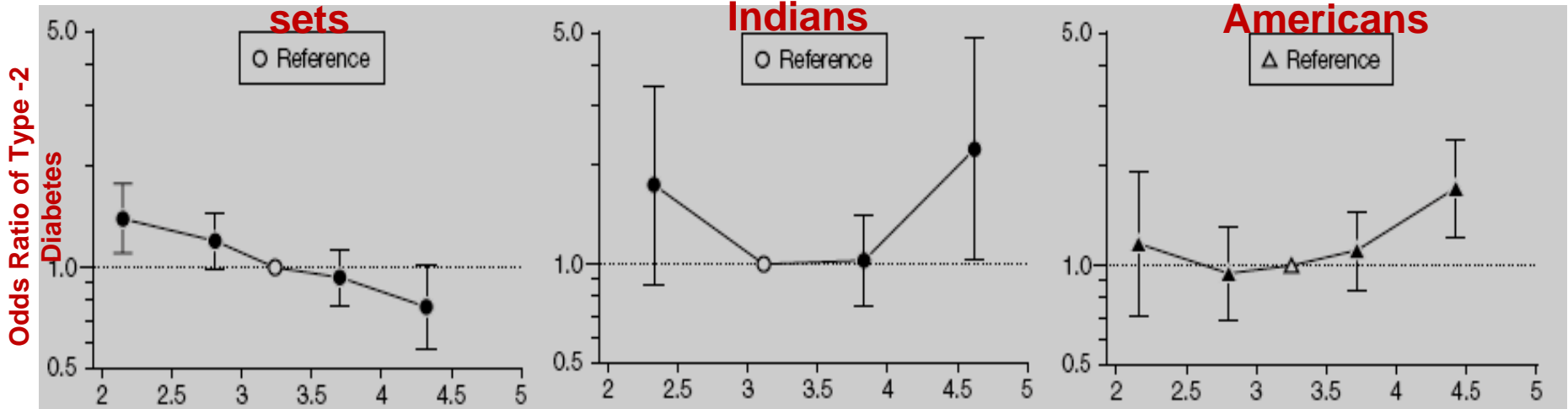
All data sets



Pima Indians

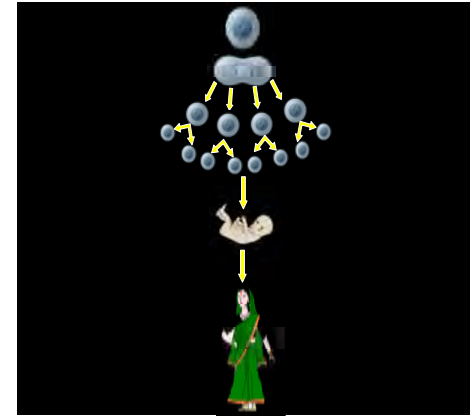


Native North Americans



Mean Birth Weight - Kg

Developmental Plasticity & Fetal Programming



➤ Ability of an organism to develop in various ways, depending on the particular environment or setting

➤ “Process whereby a stimulus applied *in utero* establishes a permanent response in the fetus leading to enhanced susceptibility to later diseases “



Alan Lucas

✓ *Metabolic, Nutritional, Temperature..*

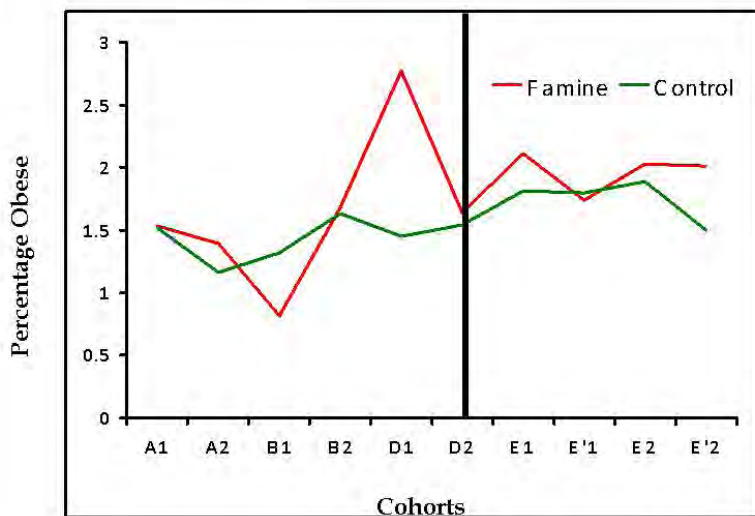
➤ Critical periods (*Windows of opportunity*)

➤ *Specificity*



Gestational Famine Exposure & Obesity

Obesity in Army Conscripts
Dutch Winter Hunger Study



Gian-Paolo Ravelli et al. N Engl J Med, 1976



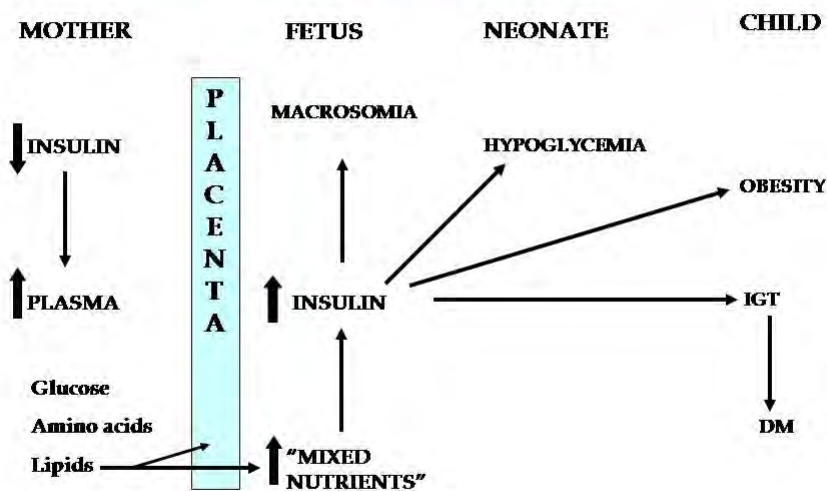
- Dutch Winter Hunger, affected and control areas
- BMI at 19y, Army conscripts
- Exposure to famine in late, mid and early gestation.
 - ✓ Late: less obesity
 - ✓ Mid and early: more obesity
- Adipocyte number
- Hypothalamic appetite centre programming

Fuel-mediated Teratogenesis

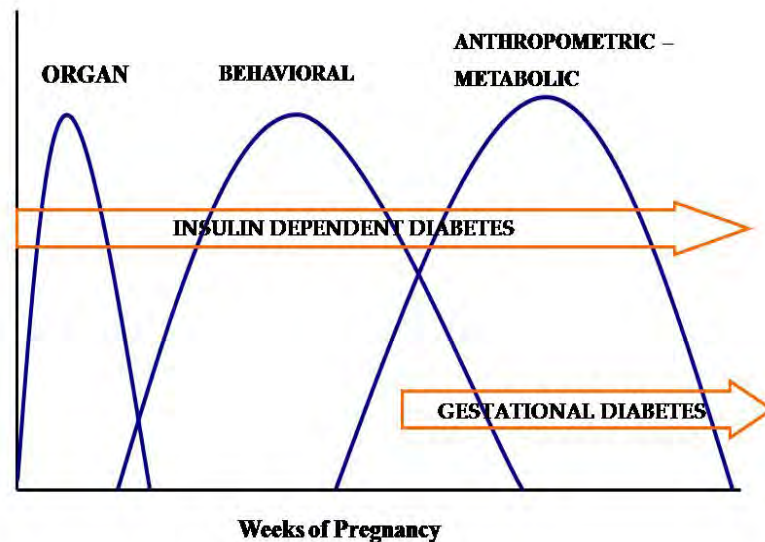
Teratology stems from the [Greek](#) τέραξ ([genitive](#) τέρατος), meaning *monster*, or *marvel*, and λόγος, meaning *speech* or, more loosely, *the study of*.

In contemporary usage, the term **teratology** generally refers to disfiguring [birth defects](#) or malformations.

PEDERSEN/FREINKEL HYPOTHESIS

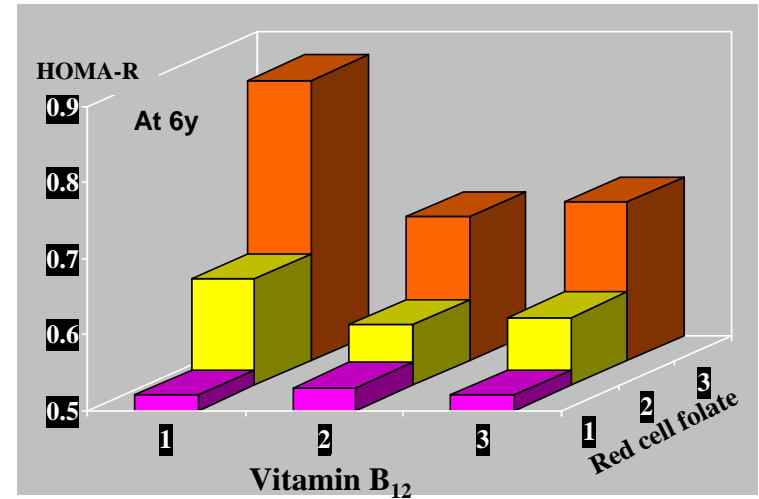
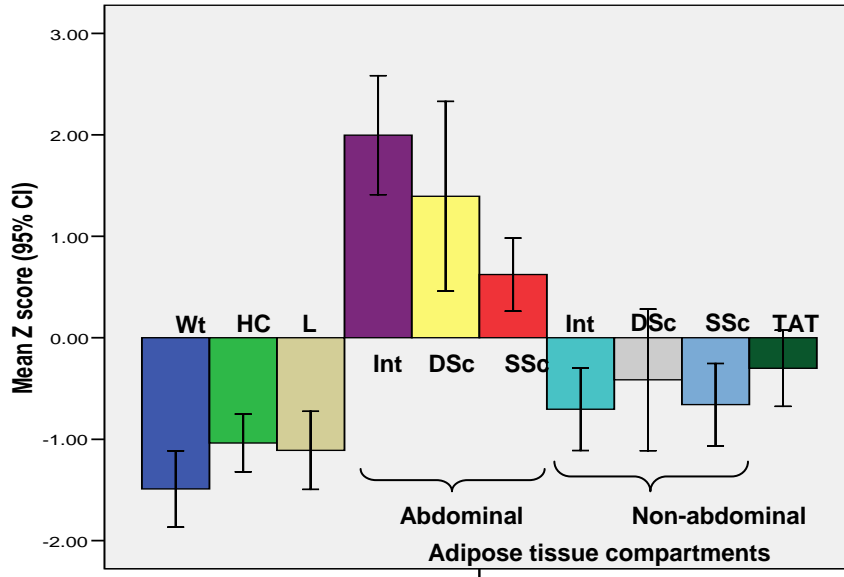


Permanant change in habitus caused by abnormal concentrations of nutrients during period of intrauterine development



Pune Studies

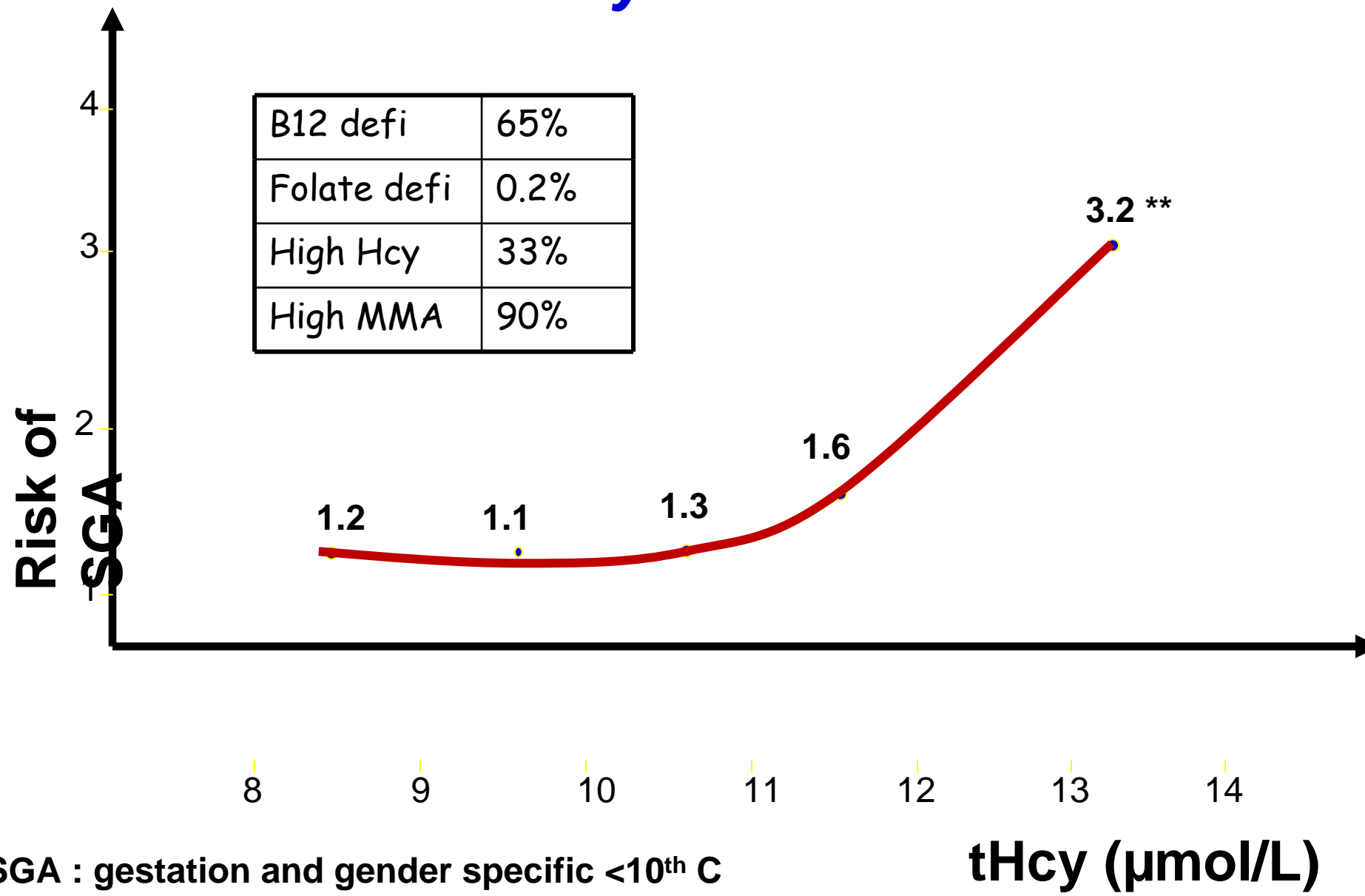
'Thin – fat Phenotype'



Yajnik CS et al JCEM 2002
 Yajnik CS et al Int J Ob, 2003
 Yajnik CS et al. Diabetologia 2008
 Modi N et al. Ped Res 2009,

Pune Maternal Nutrition Study

Maternal tHcy & Risk of SGA

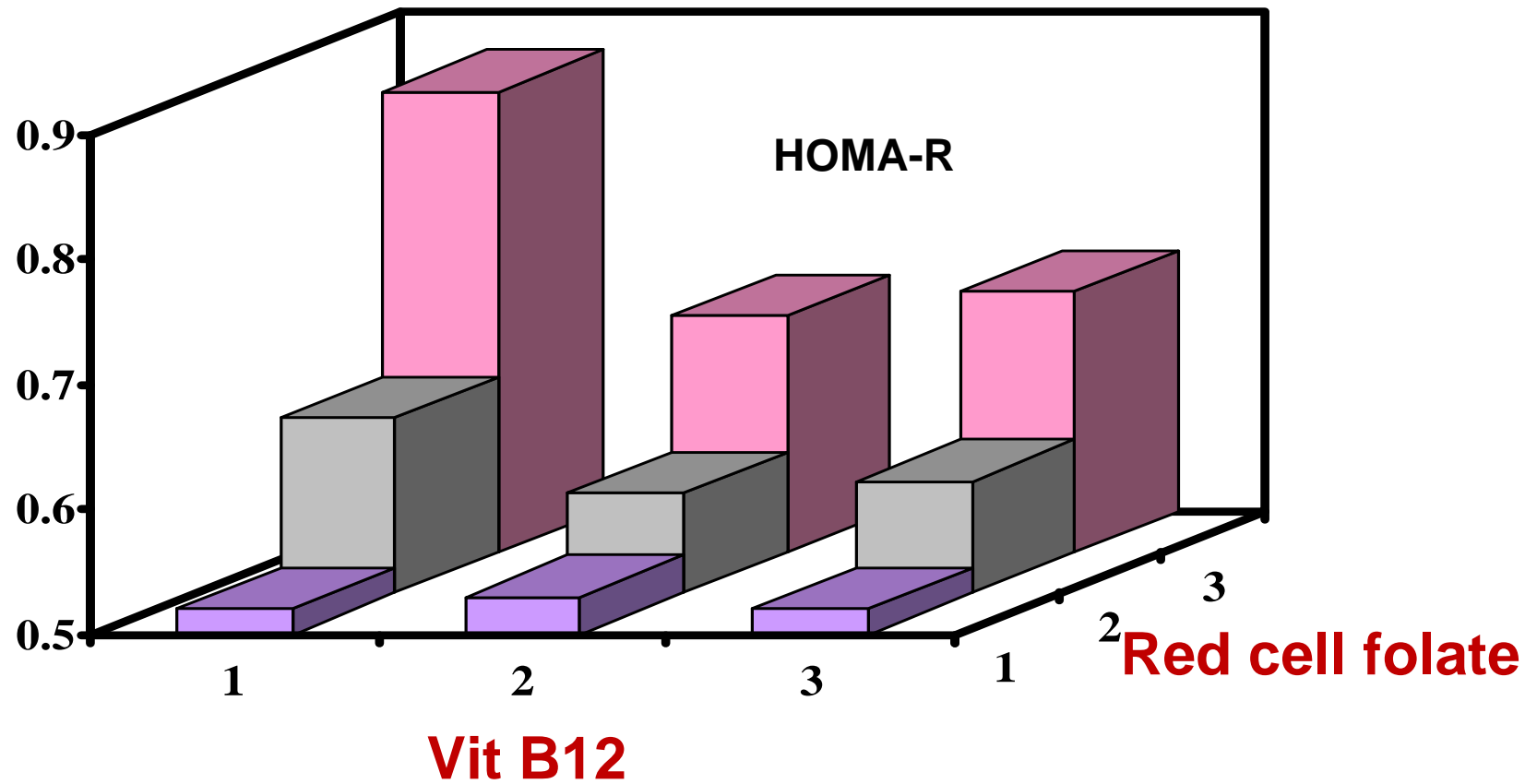


B12 defi	65%
Folate defi	0.2%
High Hcy	33%
High MMA	90%

SGA : gestation and gender specific <10th C

tHcy (μmol/L)

Maternal Vit B12 & Folate in pregnancy and Offspring HOMA-R 6y



Adjusted for sex, age and fat%; mat adiposity, protein intake, birth size, vit B12

Vegetarianism in India (B12 - Folate status)



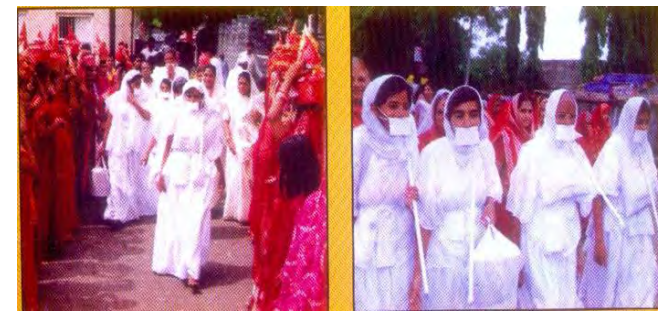
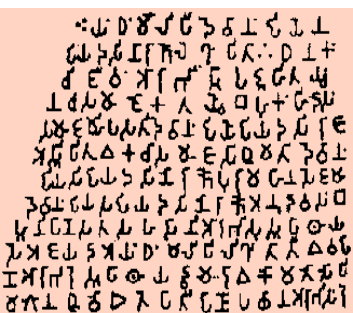
➤ **Multigenerational**

- ✓ 'Ahimsa' (non-killing), Samrat Ashok
- ✓ Religions (Jain, Hindu, Buddha)
- ✓ Education, income & hygiene

➤ **Folate 'adequacy' diet + iatrogenic**

- ✓ Higher food intake, socio-economic status
- ✓ NAPP (Iron 60mg, folic acid 0.5 mg)
- ✓ Obstetric practice: high dose folate suppl (5mg-

15mg)

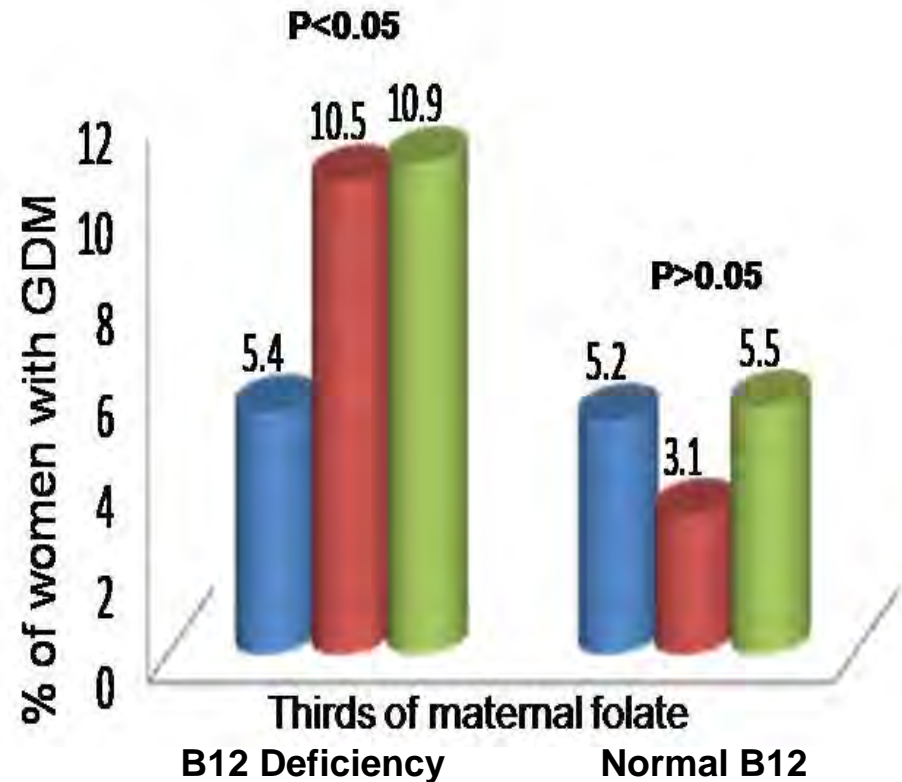
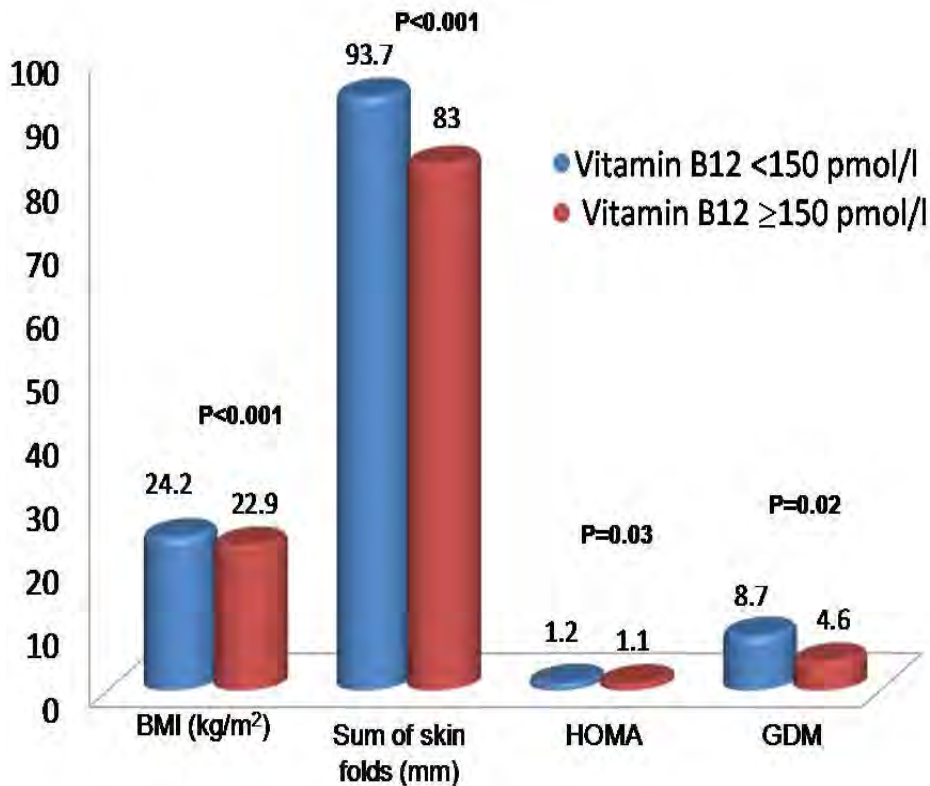


B12 deficiency and GDM

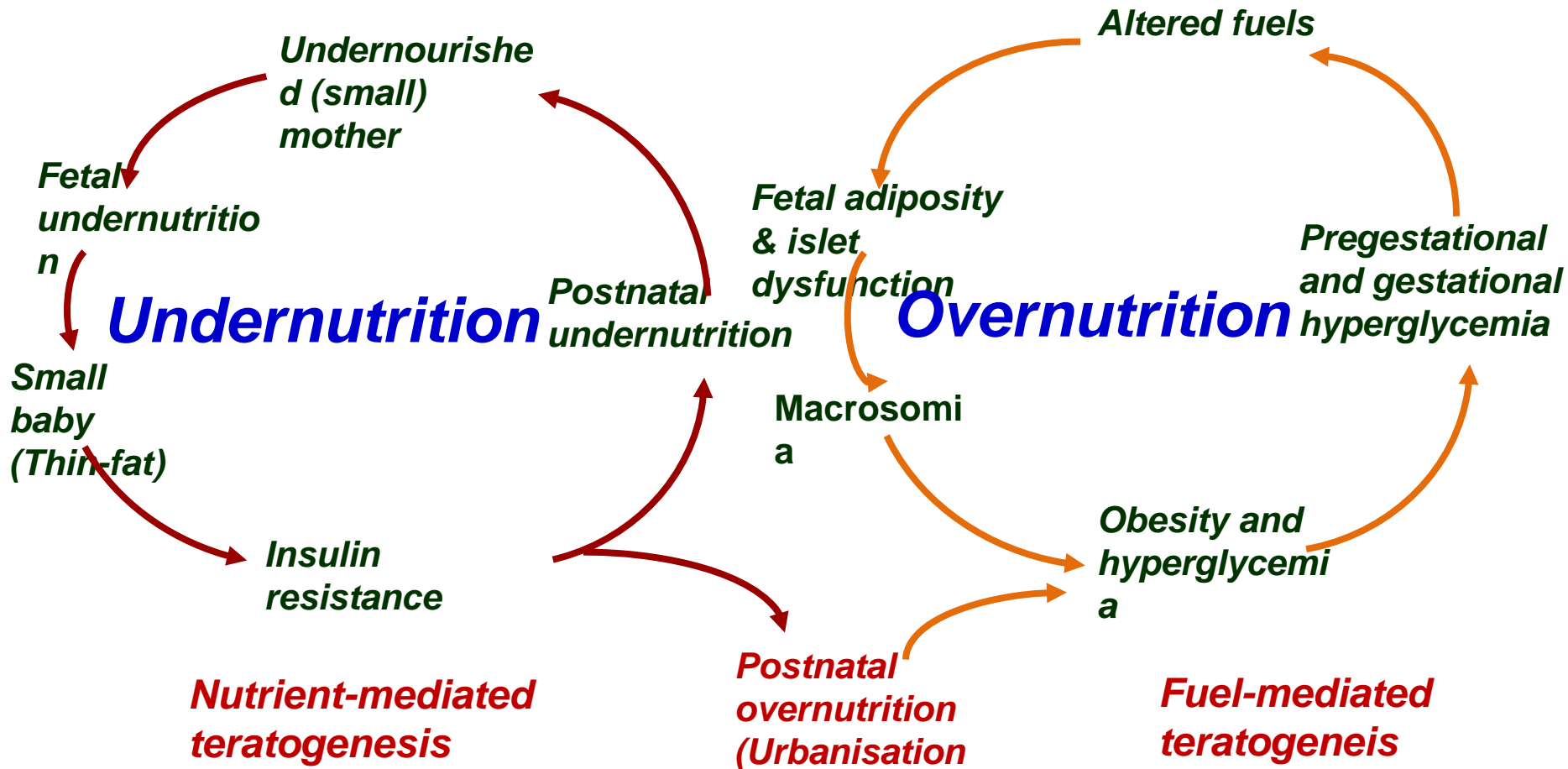
Parthenon Study, Mysore, S India

- ~800 Pregnancies
- 43% B₁₂ deficient
- 4% Folate deficient
- OGTT (100 gm)

- B₁₂ deficiency – GDM, worsened by folate
- B₁₂ deficient GDM > 2x permanent



Dual - Teratogenesis



Type 2 Diabetes

Susceptibility



**Precipitating factors
(Obesogenic)**



Accelerating factors



T2DM

- Genetics
- Fetal programming (Epigenetic)

- Lifestyle related
 - Nutrition
 - Inactivity
 - Psychosocial stress
- Rapid childhood growth
- Inflammation

- Glucotoxicity
- Lipotoxicity

Post-reproductive diabetes prevention ?



Type 2 diabetes: a result of
multi-phasic nutritional insults

The Real MRDM !
Many other !!