Maternal Diet and Fetal Growth in a Pregnancy Cohort

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With thanks to Drs. Melissa Smarr, Monica Ancira-Moreno, Marisol Castillo-Castrejon and Miatta Buxton
for slides and other background

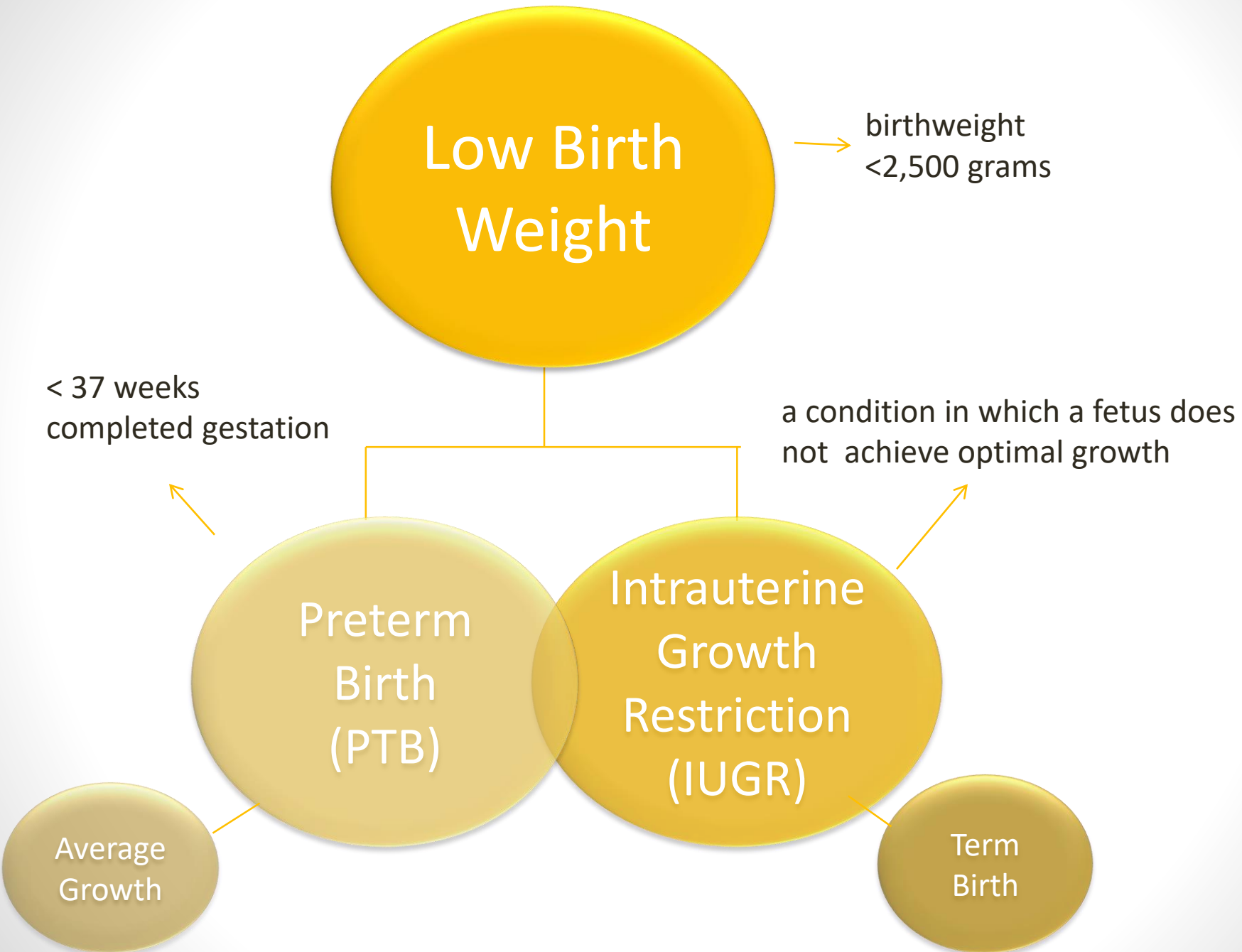**Low Birth Weight** → birthweight <2,500 grams

< 37 weeks completed gestation

a condition in which a fetus does not achieve optimal growth

Preterm Birth (PTB)

Intrauterine Growth Restriction (IUGR)

Average Growth

Term Birth

IUGR Related Neonatal Morbidity & Mortality

- Causal factor in 50% of stillbirths (Figueras et al, 2011)

- 2nd leading cause of prenatal morbidity & mortality (Peleg et al, 1998)

- Fetal mortality is 50% higher than neonatal mortality
  - Higher rates in males than females

- Neurological and mental development
  - Cerebral palsy (Illa et al, 2009)
 - ADHD (Bertino et al, 1996)

Courtesy of Dr. Felipe Vadillo

Fetal Growth Restriction

IUGR ≠ SGA

Assessment *in utero:*

- Intrauterine growth restriction (IUGR)
  - Small size and reductions in growth rate of anthropometric parameters
  - Ratios of anthropometric parameters
  - Estimated fetal weight < 10th percentile

- Distinguish between symmetric vs asymmetric IUGR
  - Increased morbidity and mortality
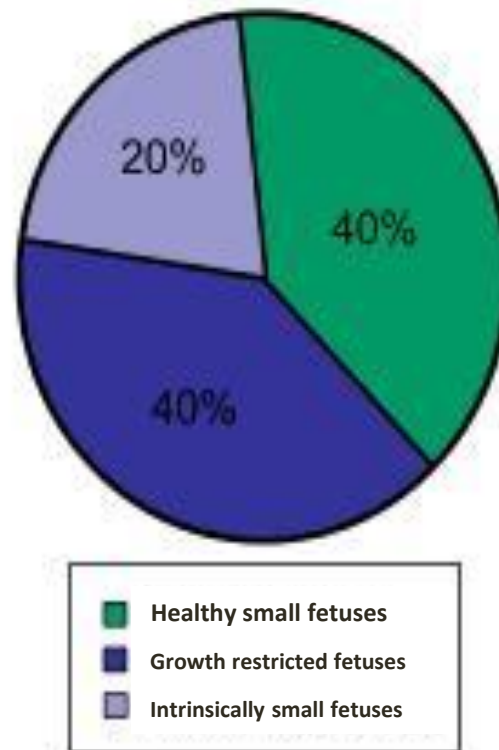
Assessment at birth:

- Small for gestational age (SGA)
  - Weight <10th percentile of age and sex adjusted population curves
  - comparisons of anthropometric parameters with population curves

- Most SGA are constitutionally small

- No increased morbidity or mortality

- 40% Healthy small fetuses
- 40% Growth restricted fetuses
- 20% Intrinsically small fetuses

Adapted from Ross et al , 2013.
http://emedicine.medscape.com/article/261226-overview

Limitations on use of birth weight

- Birth weight is not a good proxy for restriction occurring in 1st and 2nd trimesters (Hemachandra et al. 2006)

  - Intrauterine growth restriction (IUGR) ≠ SGA (Kingdom and Baker , 2000)

  - Constitutional vs Pathological growth restriction (Ananth and Vintzileos, 2009) (asymmetrical growth)

- Use of serial ultrasound measurements may help to better identify IUGR (Carrera, JM. 2001; Woodruff et al . 2009)
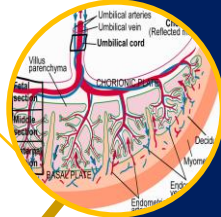
Extrinsic Risk Factors for IUGR

Health (weight, medical history), behaviors (smoking, alcohol consumption, nutritional status)

Environmental tobacco smoke, air pollutants, altitude, etc.

Placenta size, villous structure, uterine blood flow, lack of nutrients

Maternal diet and IUGR reviews

- Abu-Saad K, Fraser D. Maternal Nutrition and Birth Outcomes. Epidemiol Rev. 2010;32(1):5-25.

- Gresham E, Byles JE, Bisquera A, Hure AJ. Effects of dietary interventions on neonatal and infant outcomes: a systematic review and meta-analysis. The American Journal of Clinical Nutrition. 2014;100(5):1298-321.

- Chen X, Zhao D, Mao X, Xia Y, Baker NP, Zhang H. Maternal Dietary Patterns and Pregnancy Outcome. Nutrients. 2016;8(6).

- Grieger AJ, Clifton LV. A Review of the Impact of Dietary Intakes in Human Pregnancy on Infant Birthweight. Nutrients. 2015;7(1).

'Good' diet supports fetal growth

- "Maternal nutrition is a modifiable risk factor of public health importance that can be integrated into efforts to prevent adverse birth outcomes." (Abu-Saad et al 2010)
- "All dietary interventions and those focused on macronutrient intake also increased birth weight (P 0.01) and length (P 0.05) and reduced the incidence of low birth weight (P 0.01)." (Gresham et al 2014)
- Observational studies and randomized clinical trials support dietary intake's influence on fetal growth and birth weight.
- How do we quantify dietary intake?
  - Measured via questionnaire; daily or longer intake; create a dietary quality score or use methods like factor analysis to evaluate dietary patterns; or 'Mediterranean diet'.

Measuring Fetal Growth With Ultrasound

- Inexpensive, non-invasive 'gold standard' of growth assessment
- Fetal growth assessed by
- changes in anatomical parameters.
  - Head circumference (HC), head size
  - abdominal circumference (AC), trunk size/liver development
  - femur length (FL), overall length
  - biparietal diameter (BPD), also measures head size
- Parameter selection:
  - Reliable, well defined, easily measured, and insensitive to technical error. (Carrera et al. 2001)

Ultrasound Parameters

Head Circumference

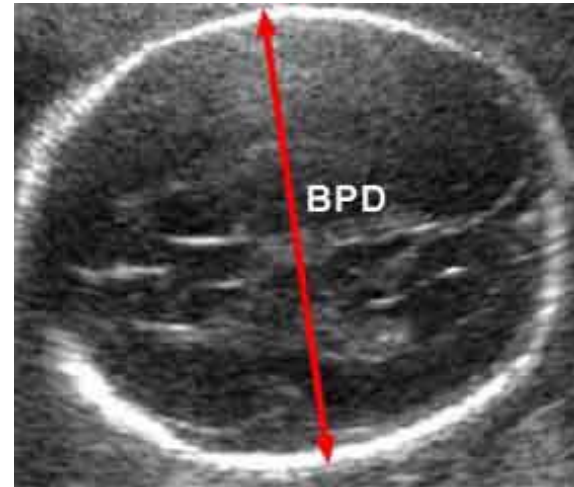Biparietal Diameter
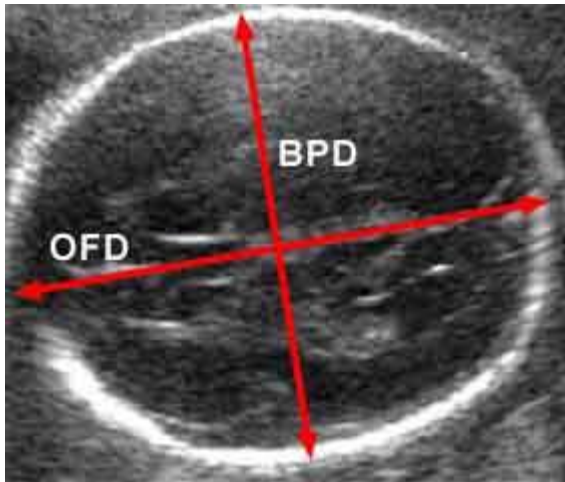
- Not commonly stalled in size or reduced in growth rate (brain sparing)

- Reduction in size and growth rate could indicate decrease blood flow to fetus (Kingdom and Baker, 2000)

- Subject to less measurement error. (Carrera et al, 2001)

- Not a good single parameter predictor of IUGR late in gestation (Carrera et al, 2001)

(Images from: Snijders & Nicolaides, 1994)

Ultrasound Parameters

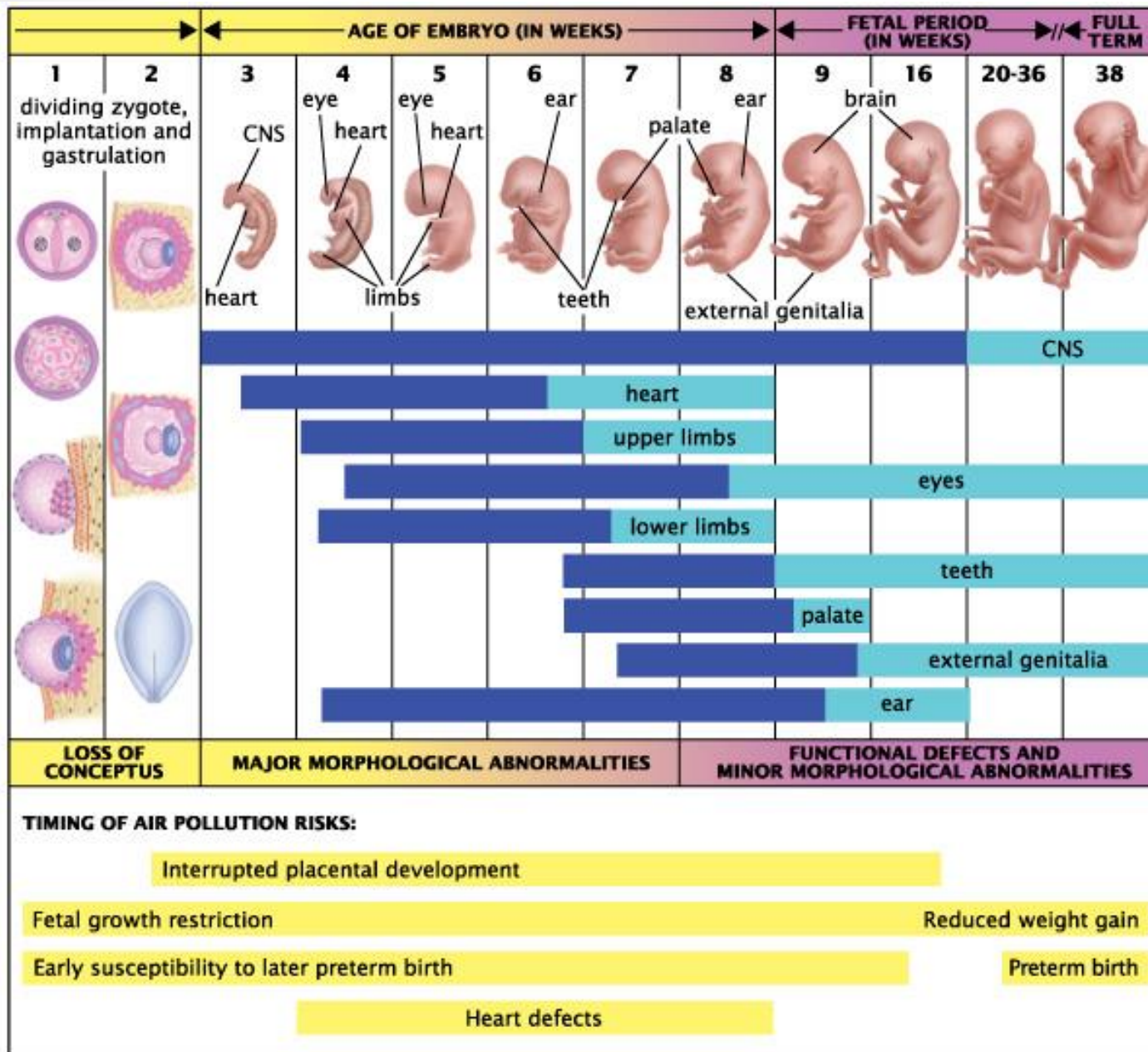Abdominal Circumference

Femur Length

- Best single parameter indicator of fetal growth ≥ 32 weeks:
  - sensitivity=83%
  - specificity = 87.7%

- Reflects volume of an incomplete liver development
(Carrera et al, 2001)
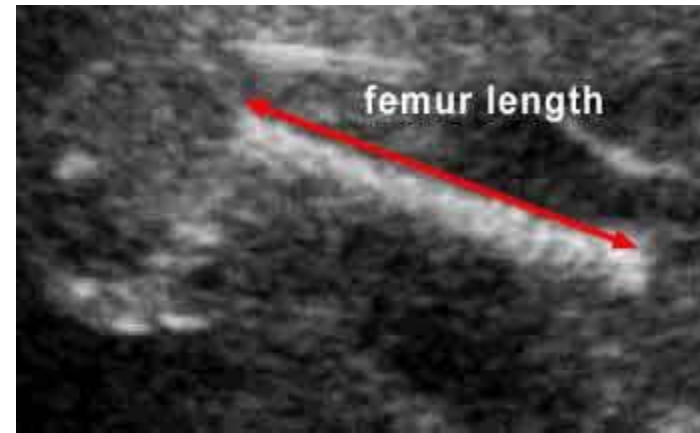
- Reductions may indicate symmetrical IUGR (Carrera et al, 2001)

- FL/AC ratio can predict growth, independent of gestational age

(Images from: Snijders & Nicolaides, 1994)

		AGE OF EMBRYO (IN WEEKS)						FETAL PERIOD (IN WEEKS)			FULL TERM
1	2	3	4	5	6	7	8	9	16	20-36	38

dividing zygote, implantation and gastrulation

CNS

eye
heart

eye
heart

ear

palate

ear

brain

heart

limbs

teeth

external genitalia

CNS

heart

upper limbs

eyes

lower limbs

teeth

palate

external genitalia

ear

LOSS OF CONCEPTUS	MAJOR MORPHOLOGICAL ABNORMALITIES	FUNCTIONAL DEFECTS AND MINOR MORPHOLOGICAL ABNORMALITIES

TIMING OF AIR POLLUTION RISKS:

Interrupted placental development

Fetal growth restriction — Reduced weight gain

Early susceptibility to later preterm birth — Preterm birth

Heart defects

Note: Blue bars indicate time periods when major morphological abnormalities can occur, while light blue bars correspond to periods at risk for minor abnormalities and functional defects.

Research questions

- Is better maternal diet quality during pregnancy associated with greater fetal growth as measured by ultrasound?
  - Is maternal weight gain a mediator of this association?
- Does the association between maternal diet quality during pregnancy and fetal growth depend on the mother's pre-gestational body mass index (BMI)?

Research Importance & Implications

- Use of repeated ultrasound measurements of fetal anthropometric parameters may reduce misclassification of growth restriction compared to SGA measure

- Better understanding of extrinsic risk factors of IUGR (e.g., nutrition) could help with education around maternal health behaviors

- Early identification of IUGR could set the course for treatment and management, reducing the number of IUGR attributed still births and low birth weight infants

Study Population

## Pregnancy Research on Inflammation, Nutrition, & City Environment: Systematic Analyses (PRINCESA) Cohort

- Live and work in Mexico City

- Age ≥ 18 years

- Most were non-smokers and recruited
  < 18 weeks of gestation

- Singleton pregnancy

- Other study design details in O'Neill et al., 2012

CURRENT SAMPLE: 660 women with live births

- Location: Valley of Mexico
- Altitude: 2,240 meters
- Population: 21 million
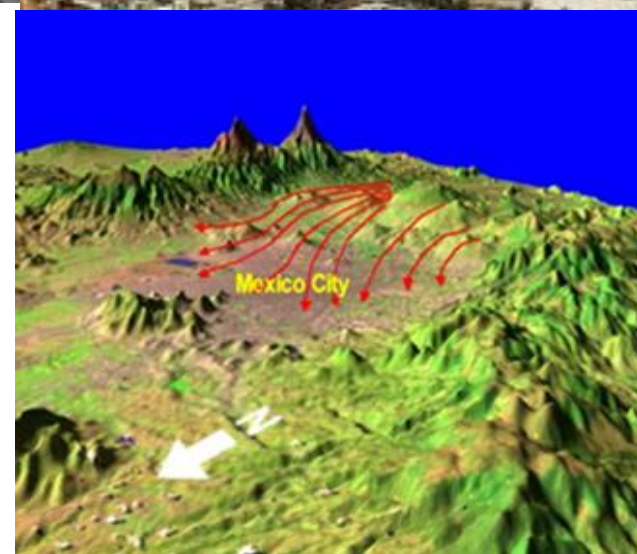
Flow of data collection

Baseline:

1. Informed consent
2. Demographics
3. Health history

Monthly visits:

1. Clinical evaluation: **fetal growth assessment with ultrasound**, other clinical data.

2. Maternal anthropometric measures, weight gain

3. Nutritional assessment: Food frequency questionnaire (FFQ) and 24 hour recall.

Dietary intake

At one to three visits during pregnancy, we administered a quantitative assessment of dietary intake

- Multi-step 24-hour dietary recall → quantitative

    Use of food replicas

    Analyzed by Food Processor®

- Calculated:

Maternal Dietary Quality
Score (0 to 6, from food groups)
over the entire pregnancy

Variables of interest from Mexico City PRINCESA cohort

Repeated Fetal Ultrasound Data

- Head Circumference (HC)

- Biparietal Diameter (BPD)

- Abdominal Circumference (AC)

- Femur Length (FL)

Maternal Questionnaire Data

- Maternal age
- Parity
- Education
- Marital status
- Maternal height
- Pre-pregnancy BMI
- Nutrition (MDQS)
- Total energy intake
- Maternal weight gain (repeated measures)
- Baby's sex

THANK YOU!
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