The Chiba Study of Mother and Children's Health (C-MACH) and Pediatric Allergy in Japan

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Developmental Origins of Health and Disease (DOHaD)

Some epidemiological studies have shown that environmental factors, such as maternal nutrition, smoking habits, and economic stability during the period from fetal development to early childhood stage, might affect the risk of non-communicable diseases in adulthood.

Chemical exposure (PCBs, metals etc)

Smoking

Nutrition

Genetic background

Social factors (Income etc)

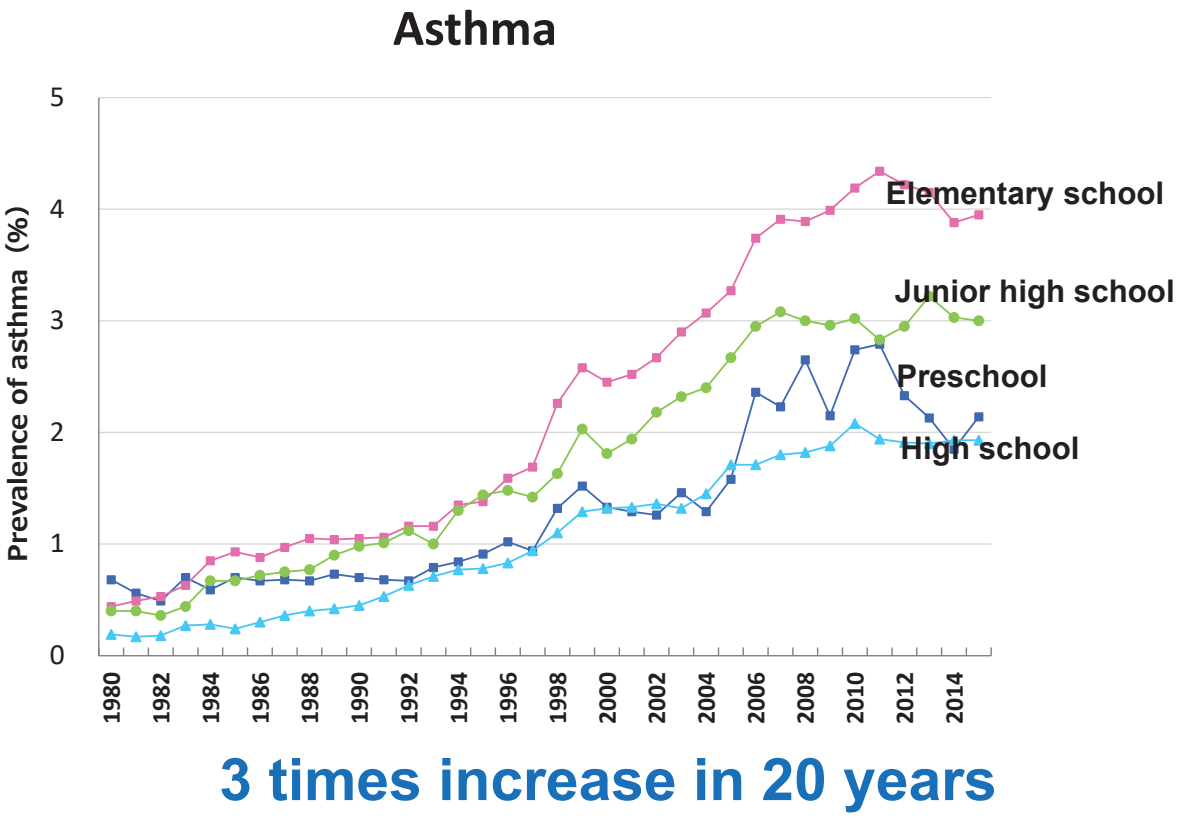
Disruption of biological system

Metabolic pathways
Metagenome

Increased risk of developing post-natal disease or lifestyle disease after adult?

Barker, D. J., & Osmond, C. (1986). The Lancet, 327(8489), 1077-1081.
Osmond, C., & Barker, D. J. (2000). Environmental Health Perspectives, 108(Suppl 3), 545.

Increase of children's allergies in Japan



3 times increase in 20 years

From: school health statistics

Causes **of allergies**

Genetic factor

Living Environment

Allergen

food

mite

mold

pollen

Animal hair etc.

virus

stimulation

tobacco smoke

Air pollution

weather

hard exercise

stress

Life-style etc.

Center for Preventive Medical Sciences, Chiba University

If exposure is prevented by scientific efforts, adverse effects can be prevented for future generation.

Well designed large scale birth cohort study will lead us to the core of the issue and will prevent possible adverse effects of environmental factors such as chemical exposure

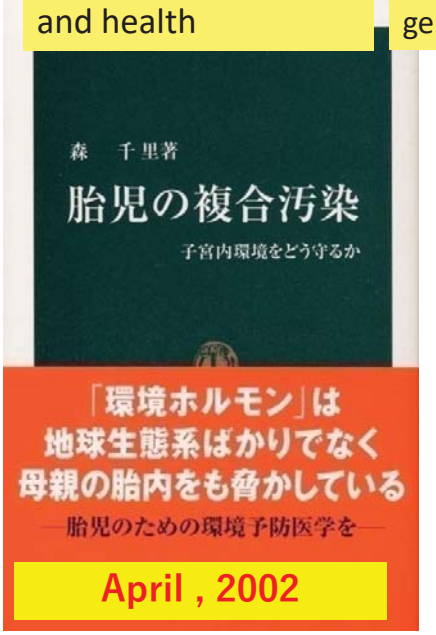


Publication of textbooks for education

Books such as fetal exposure issues or birth cohort

We proposed the concepts of "Environmental Preventive Medicine for Future Generations"

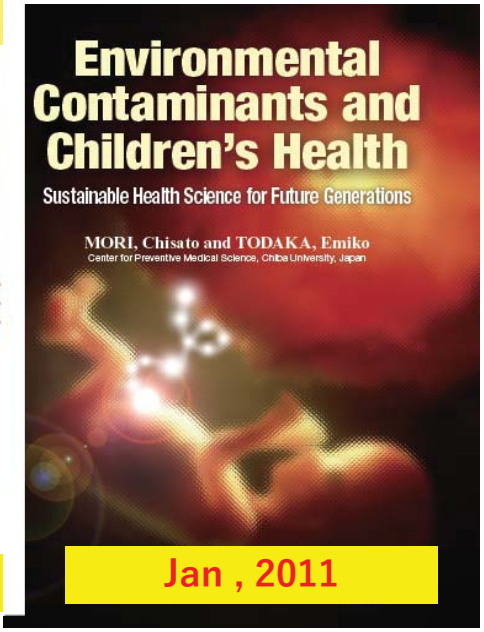
Fetal exposure to multiple chemicals and health



April , 2002

Umbilical cord tells multiple contamination and future generation's health

May , 2008



Jan , 2011

Effects of fetal environment on children's health

JECS
National 103,099 Chiba 6,191

C-MACH
408

Large cohort
- National data analysis
- Various environmental factors
- Serial health assessment of child

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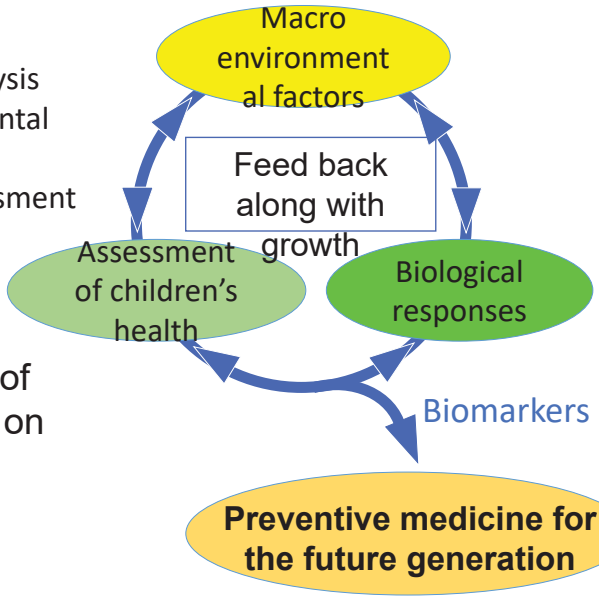
To clarify effects of fetal environment on their health



Analysis of biomaterials
- Maternal blood, cord blood, umbilical cord (mesenchymal cells), breast milk, feces (mother and child)

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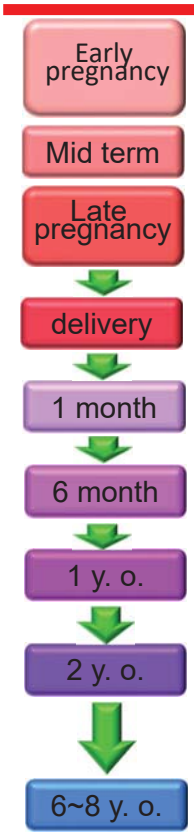
Association between environmental factors and epigenome, metagenome, and metabolome

Environ Sci Pollut Res Int (2015)

BMJ Open (2016)

Birth Cohort in Chiba

Hospital-based cohort study



Fathers Mothers

Saliva

- Blood
- Urine
- Feces
- Milk
- Questionnaire
- Medical record

Children (400～500)

- Placenta
- Cord
- Cord blood
- Meconium
- Feces
- Urine
- Teeth
- Medical record

Open Access Cohort profile

BMJ Open Chiba study of Mother and Children's Health (C-MACH): cohort study with omics analyses January 30, 2016

- **Research on environment from fetal to infant period (Exposure to chemicals, lifestyle, food, psychological and social factors)**
- **Epigenomic analysis**
- **Biomarker/indicator analysis**
- **Intestinal microflora analysis**

- **Follow the low birth weight babies（DOHaD）**
- **Research on allergies, neurodevelopmental disorders**
- **Research on the causes of the above**

C-MACH

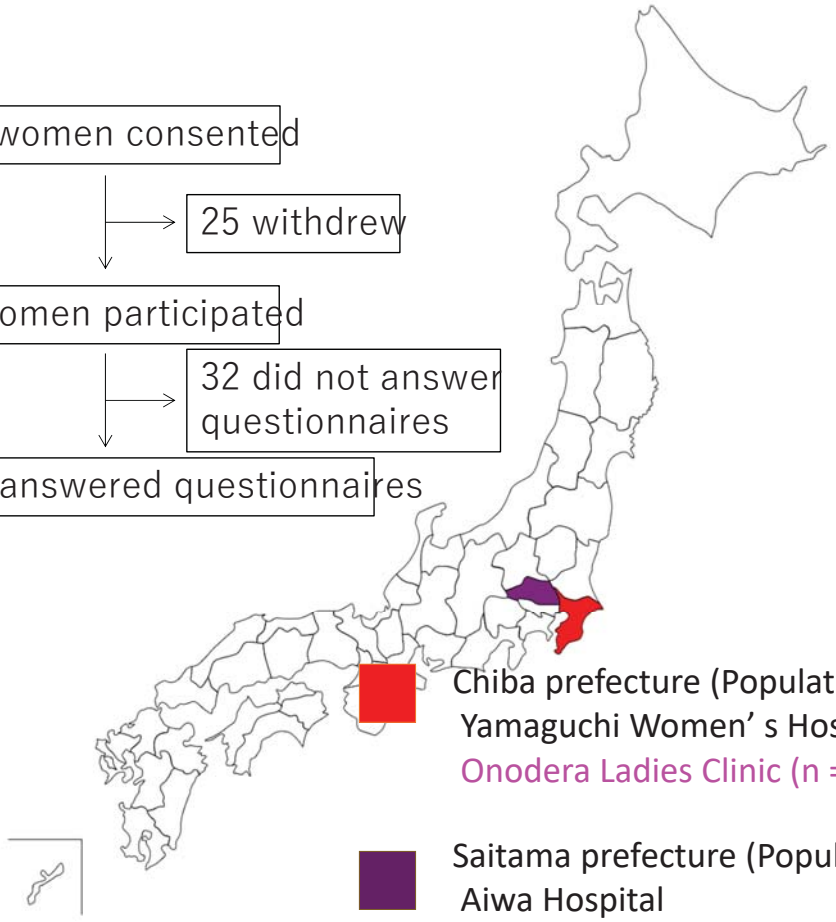
433 women consented

→ 25 withdrew

408 women participated

→ 32 did not answer questionnaires

376 women answered questionnaires



Chiba prefecture (Population: 6.2M)
Yamaguchi Women' s Hospital
Onodera Ladies Clinic (n =93)

Saitama prefecture (Population: 7.2M)
Aiwa Hospital

Microbial environment during pregnancy and the dermatitis in early infancy of their children: a pilot study of C-MACH

Background and hypothesis:

1. The prenatal maternal microbial environment, including the gut microbiota, has been suggested to influence the incidence of allergies in the offspring.
2. Epidermal barrier dysfunction in early infancy has been attributed to the development of subsequent allergies.
3. Prenatal microbial environment may affect the gut microbiota, acting as an initial trigger to alter immune development of the foetus.
4. The maternal microbial composition might be linked to the prevalence of dermatitis in early infancy of the offspring, leading to subsequent allergic symptoms.

TANABE H et al; World Allergy Organization Journal (WAOJ) 2019

Subjects and methods

434 healthy pregnant women at <13 weeks' gestation

Dermatitis in early infancy was assessed up to 4 months after birth

Allergic symptoms such as wheeze, dermatitis were assessed from the answers in 10-months questionnaire.

Other information related to the maternal microbial environment was obtained from the questionnaires during pregnancy.

Stool samples were collected from mothers at the hospitals at 12 (*n* = 59) and 32 weeks (*n* = 58) of gestation, and the gut microbiota were analysed based on barcoded 16S rRNA sequencing.

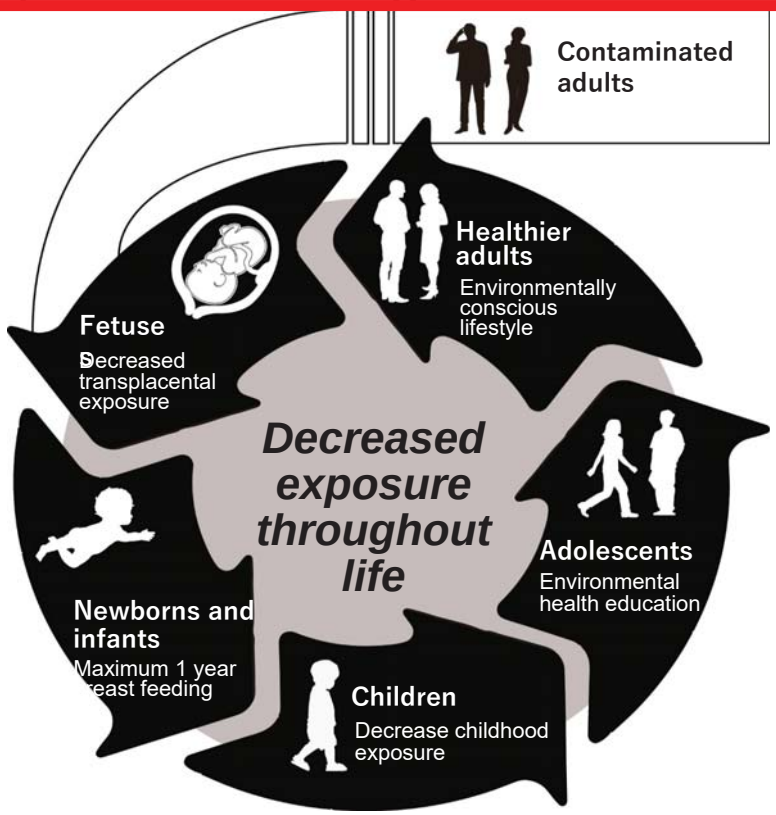
Tanabe H et al; 2019

Conclusions

1. The prenatal maternal microbiome composition influences the occurence of allergies in the offspring.
2. The diversity of Proteobacteria and the relative abundance of Actinobacteria in prenatal faeces negatively associated with dermatitis in early infancy, which predispose the foetus to subsequent allergies in infancy.
3. This early trigger could be a good predictor of subsequent allergies and an allergic march through infancy and childhood.

If this cycle became implemented, it would be possible to produce healthier future generations.

Virtuous Cycle for Reducing Environmental Exposure



Mori and Todaka; For a healthier future: a virtuous cycle for reducing exposure to persistent organic pollutants **JECH Online First, published on May 17, 2017 as 10.1136/jech-2016-208088**

Thank you for your attention!

If exposure is avoided, adverse health effects and diseases could be prevented for future generations

"In Our Every Deliberation, We Must Consider the Impact of Our Decisions on the Next Seven Generations"

From "Great Law of the Iroquois Nation"