

超党派 成育医療等基本法成立に向けた議員連盟勉強会
於:参議院議員会館
2018.08.29

世界から危惧されている次世代の健康リスク (ドーハッド(DOHaD)説の示す警告)

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日本DOHaD学会代表

福岡秀興

(ドーハッド)DOHaD

(Developmental Origins of Health and Disease)

成人病胎児期発症起源説

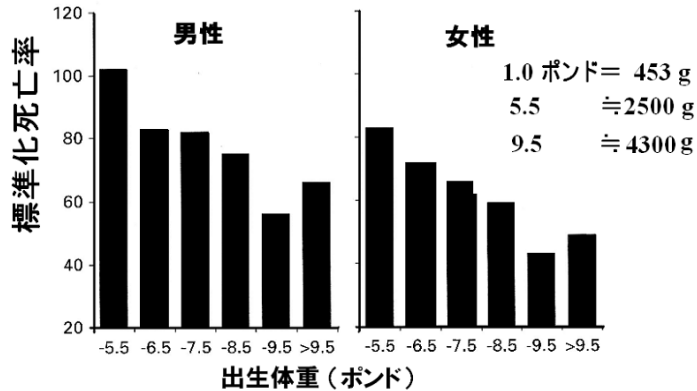
(Fetal origins of Adult Disease:FOAD)

“成人病(生活習慣病)の素因は、受精時、胎芽期、胎児期、乳児期に遺伝子と環境との相互関連で形成され、出生後のマイナス生活習慣の負荷で成人病が発症する。疾病はこの二段階を経て発症する。素因とは**エピジェネティクス**偏移である。(David Barker. 1986.)

(Transgenerational effect : 世代を超えた伝達現象)

国際DOHaD学会、日本DOHaD学会

出生体重と虚血性心疾患死亡率の相関



Osmond C. D. Barker, *BMJ* 307: 1519, 1993

胎内低栄養曝露によるShizophrenia・成人病の多発

(*natural experiments*)

1) オランダの冬の飢餓事件

(Dutch Hunger Winter Famine: 1944.11. -1945.4.)

Stein Z et al. *The Dutch Hunger Winter of 1944-1945.*
Oxford University Press; 1975

2) 中国の大躍進

(The Great Leap Forward in China: 1959 - 1961)

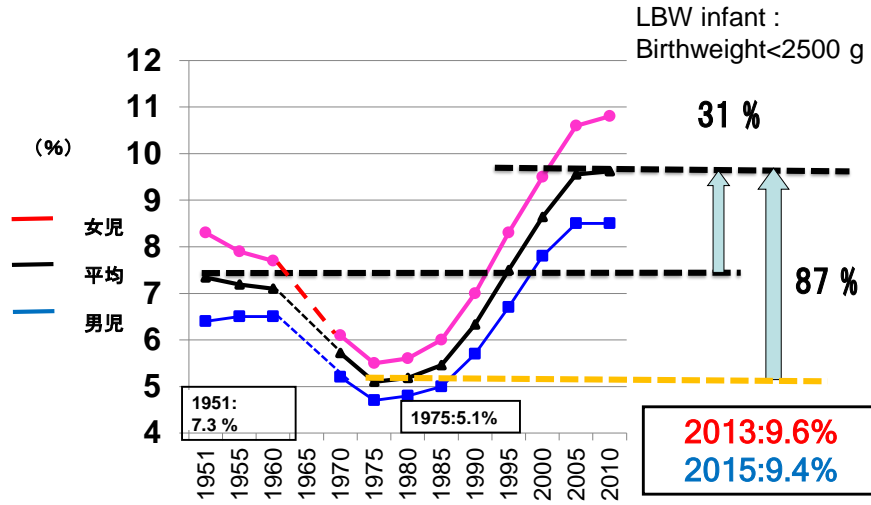
St.Clair D, et al., *JAMA* 2005; 294: 557

出生体重低下による発症リスクが上昇する疾患

- 1) 高血圧・心臓循環器疾患
- 2) 耐糖能異常・II型糖尿病
- 3) メタボリック症候群
- 4) 骨粗鬆症
- 5) 脂質異常症
- 6) 精神神経発達異常
- 7) 慢性閉塞性肺疾患
- 8) 初経・閉経の早期化
- 9) SGA性低身長
- 10) 妊娠合併症
- 11) その他

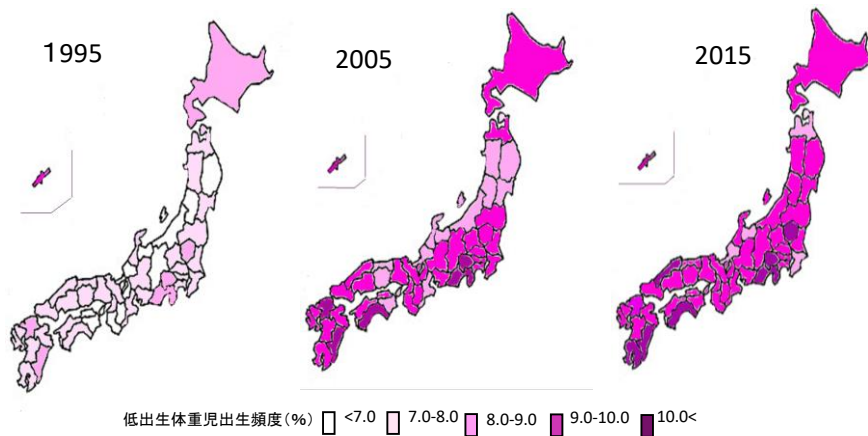
日本の現況

低出生体重児頻度の推移 (5年毎:1951-2010)



「母子保健の主たる統計」より

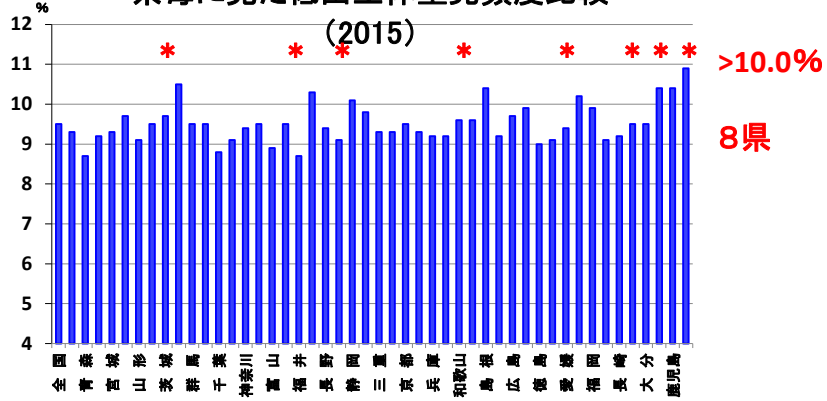
県別に見た低出生体重児出生頻度の推移



(新井孝子先生作成)

厚生労働省 人口動態調査上巻 出生 都道府県 性別にみた出生時の平均体重及び2500g未満の出生数及び割合より作成

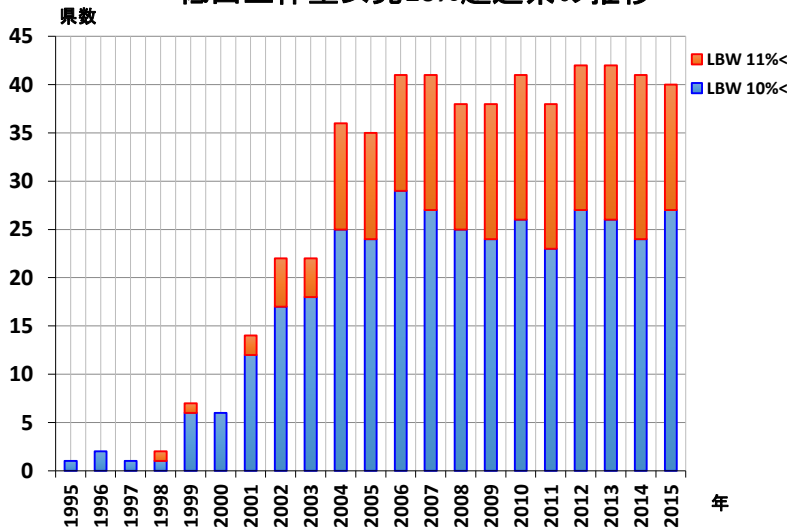
県毎に見た低出生体重児頻度比較



新井孝子先生作成

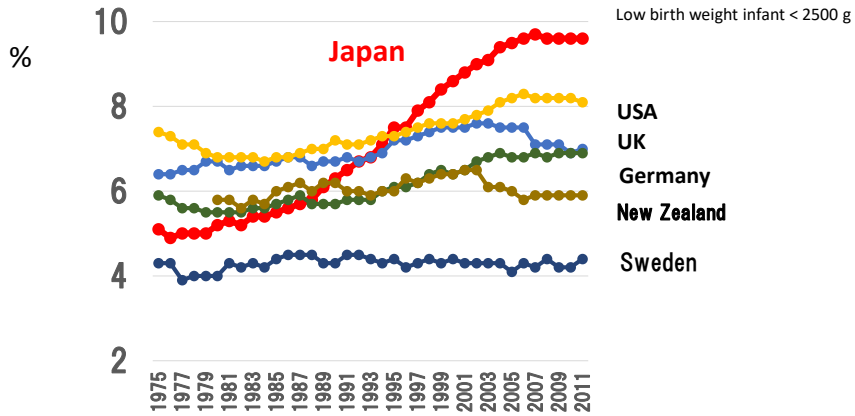
厚生労働省 人口動態調査上巻 出生 都道府県 性別にみた出生時の平均体重及び2500g未満の出生数及び割合より作成

低出生体重女児10%超過県の推移



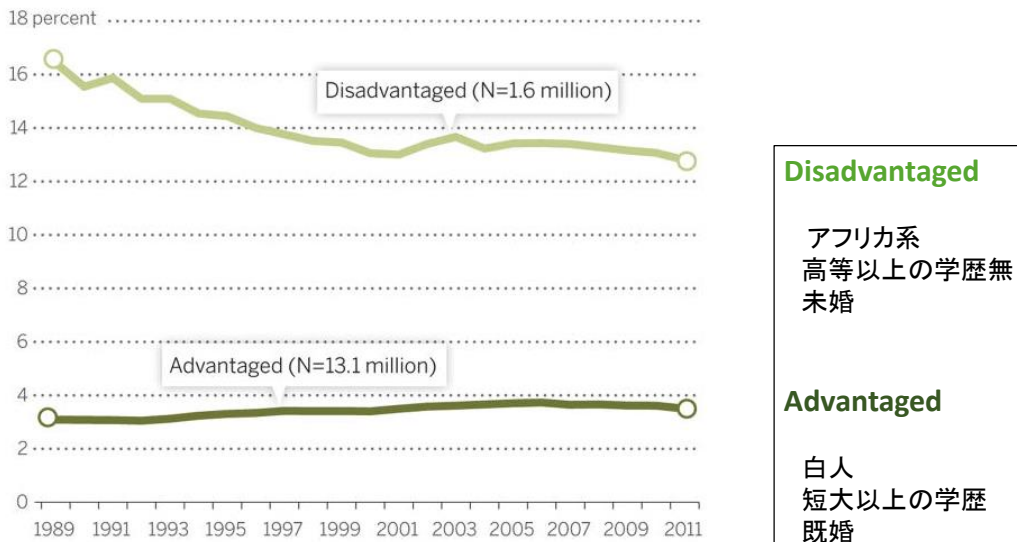
厚生労働省 人口動態調査上巻 出生 都道府県 性別にみた出生時の平均体重及び2500g未満の出生数及び割合より作成

低出生体重児頻度の推移 (1975-2011)



OECD Health Statistics (2015)より
佐田文宏氏作成

低出生体重児頻度(%)の米国推移



[Aizer A., Currie J., Science. 2014 ; 344\(6186\): 856-861.](#)

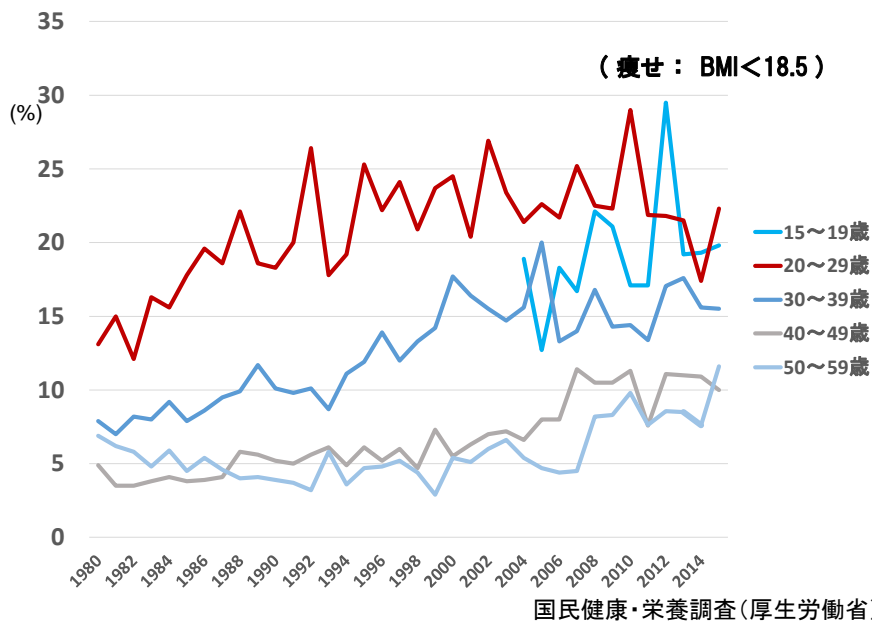
先制医療

ライフコース・ヘルスケアは
社会と健康の概念を変革する医療
～個の予防としての「先制医療」は胎生期から～

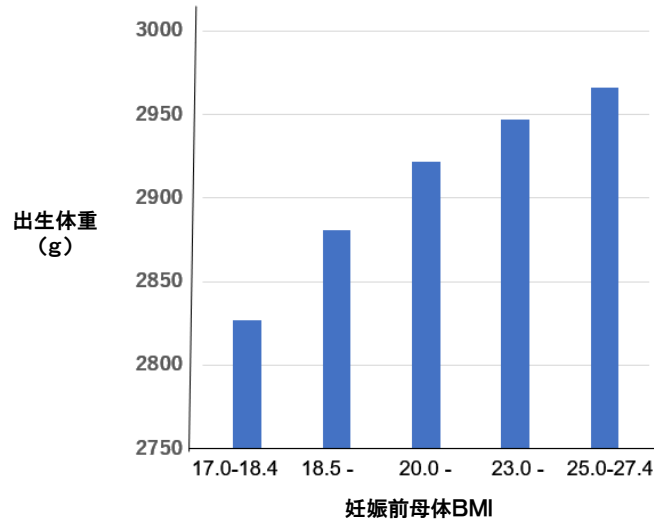


井村 裕夫氏
京都大学名誉教授

「痩せ女性」頻度の推移

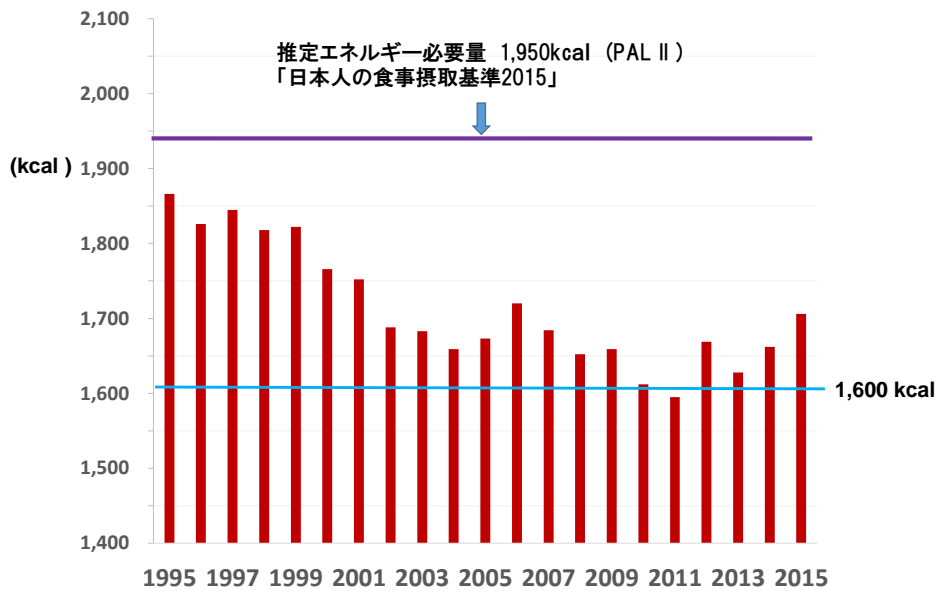


妊娠前母体BMIにそが出生体重規定する要因



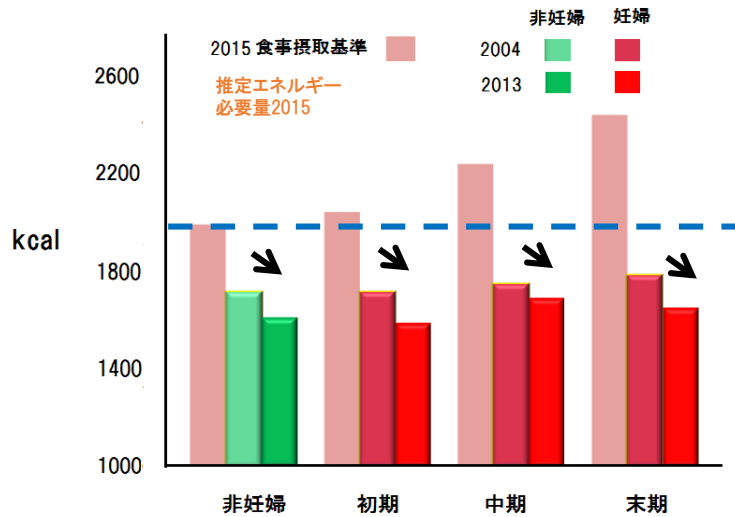
Morisaki N., J Epidemiol 2017. 27,249より作成

20代女性のエネルギー摂取量の推移



国民健康・栄養調査(厚生労働省)

妊娠中のカロリー摂取の推移



妊婦推定エネルギー必要量(食事摂取基準2015)と現実(kcal)

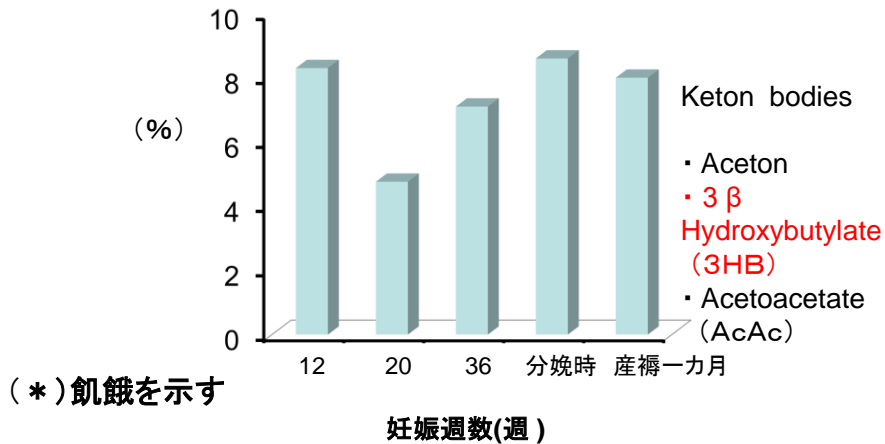
(18-29歳 身体活動レベルII)

| | (付加量) | (必要量) | 調査結果(SD) |
|----|-------|-------|--------------------|
| 初期 | 50 | 2,000 | 1,580 (380) |
| 中期 | 250 | 2,200 | 1,580 (350) |
| 末期 | 450 | 2,400 | 1,550 (340) |

Kubota K, et al., J Obstet Gynecol Res 2013;39: 1383

合併症のない妊婦のケトーシス(*)の頻度

(3HB+AcAc > :124 μ mol/L)

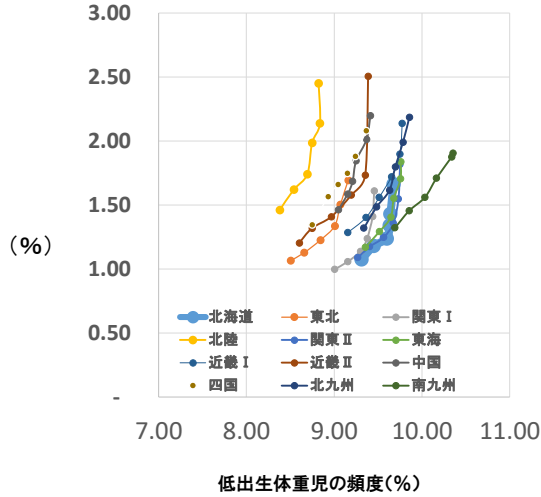


日本の知見の一部(紹介)

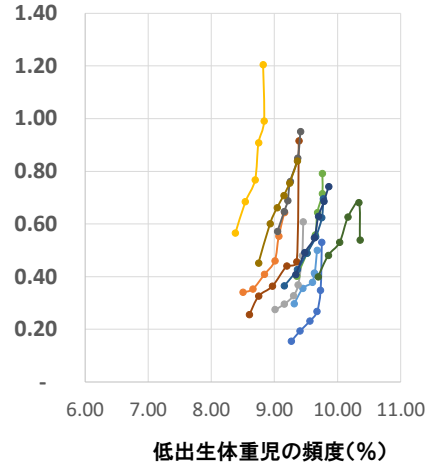
- 1) 発達障害の増加
- 2) 小児NAFLDの増加
- 3) 学力、体力の低下
- 4) 先天奇形の増加
- 5) クル病、頭蓋ろうの増加
- 7) 体格の低下傾向
- 8) 思春期発来及び閉経の早期化
- 9) 妊娠合併症(妊娠高血圧症候群、妊娠糖尿病)

低出生体重児頻度と小学生発達支援（12ブロック:H20-29）

(通級+学級)知的障害

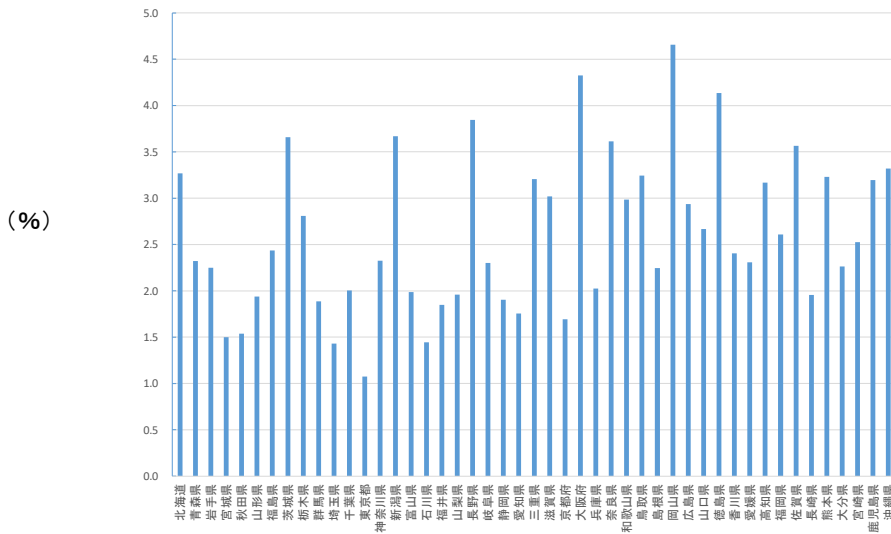


(通級)自閉症・学習障害・注意欠陥多動性障害



出典:文部省学校基本調査 H20~H29
 小学校都道府県別 種類別特別支援学級児童数
 小学校都道府県別 学級編成方式別児童数

知的障害または情緒障害(H29)



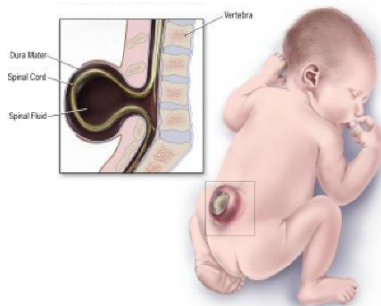
文部省学校基本調査 H29
 小学校都道府県別 学級編成方式別児童数
 情緒障害は表のままの数字で定義は文部省

二分脊椎症が増えている？

葉酸摂取の不足のみが原因か？

神経管閉鎖障害 (NTDs : Neural tube defects)

二分脊椎症

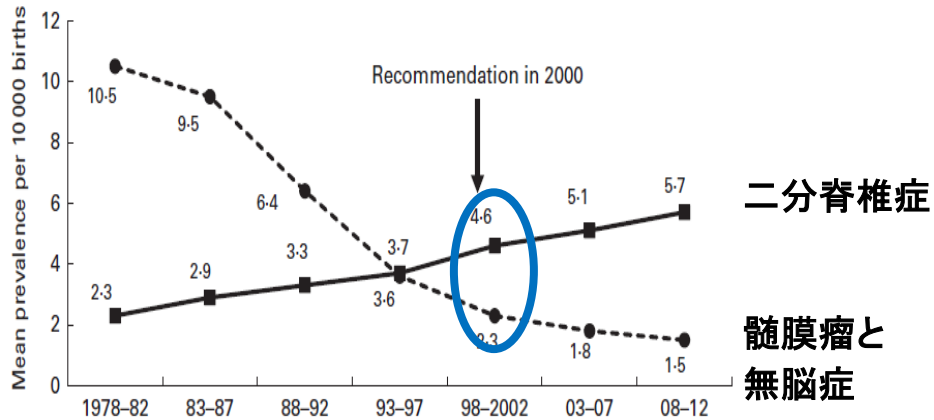


無脳症



CDC-NCEH99-0463

日本での二分脊椎症と無脳症・髄膜瘤の推移
(per 10,000 births in Japan)

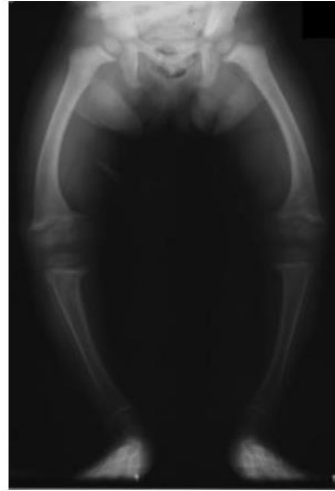


Kondo A., et al. Brit J Nutri 2015; 114:84-90

小児クル病が増えている
?

(ビタミンDは骨Ca代謝のみ?)

クル病

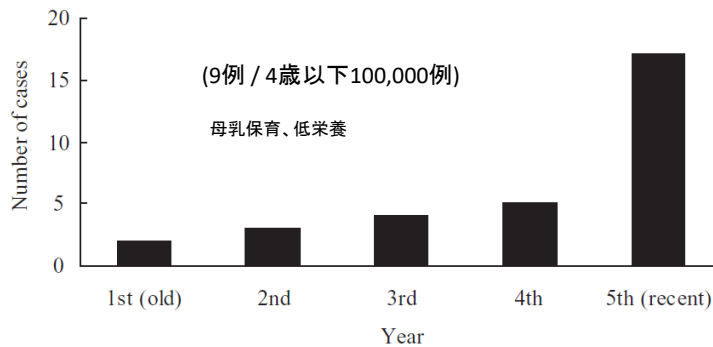


<http://www.orthopaedicsone.com/display/Classification/Define+and+contrast+osteoporosis+and+osteomalacia>

Michael Richardson: Xray RicketsLegssmall.jpg

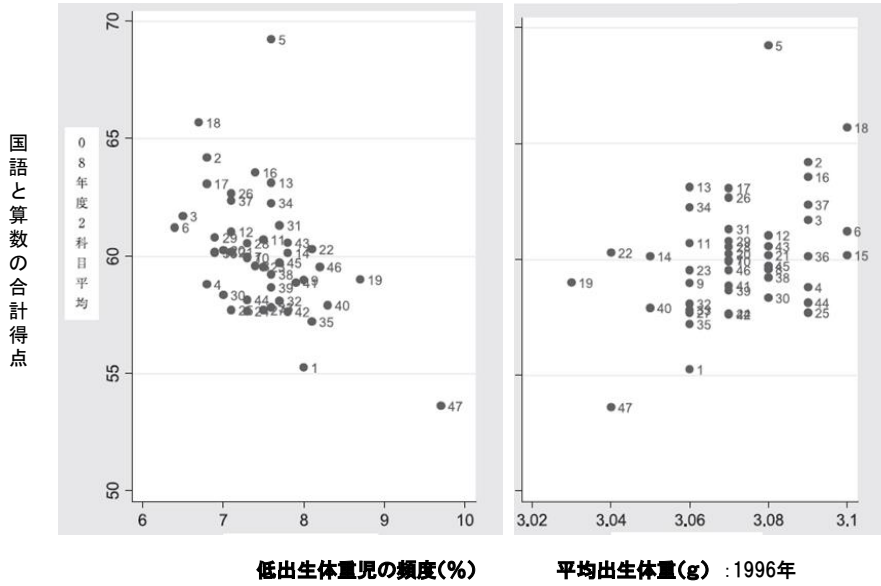
北海道における年間クル病報告数

(from July 1999 to June 2004)



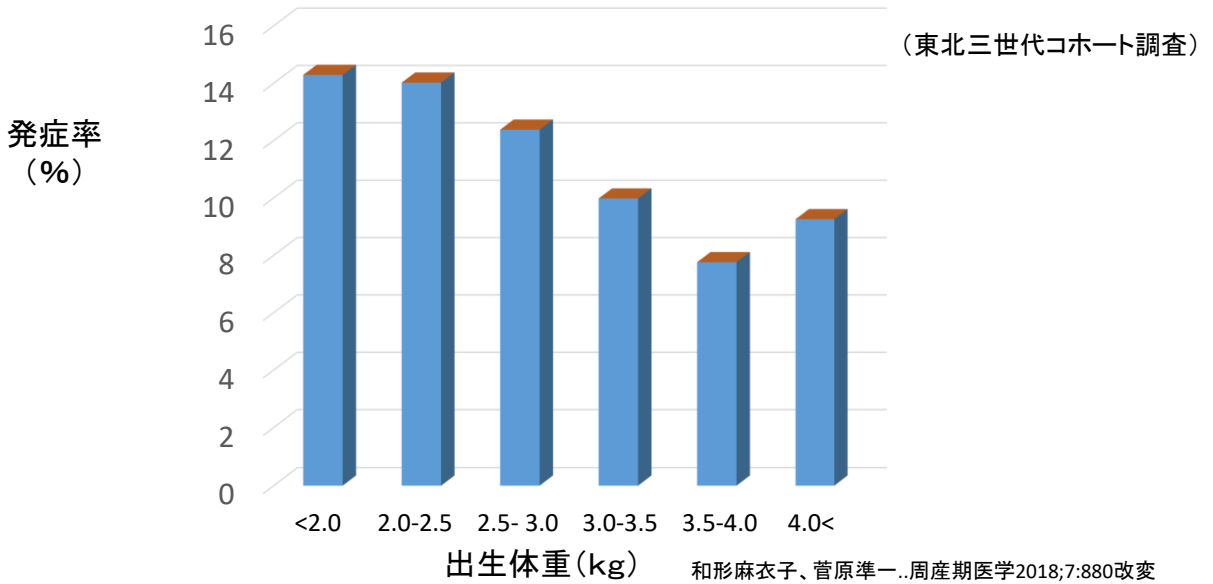
Matsuo k., Pediatrics International (2009) 51, 改変

県毎にみた学力と低出生体重児の頻度及び平均出生体重の関連
(小学6年生:2008年度)



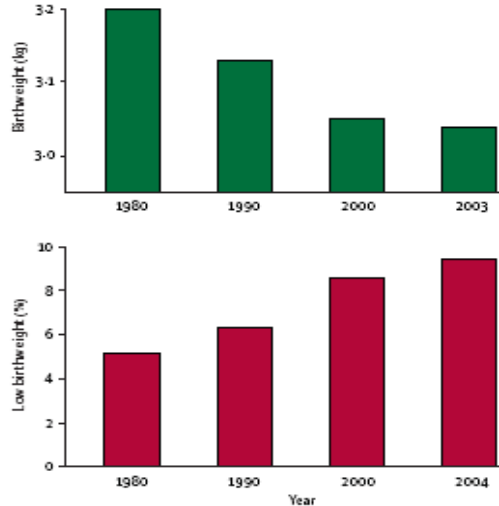
小原美紀、大竹文雄.子供の教育成果の決定要因.日本労働研究雑誌 2009;588:67.

母親出生体重から見た妊娠高血圧症候群の発症リスク



(warning from abroad)
Birth weight is falling in Japan

Trends in mean singleton birthweight (upper panel) and mean prevalence of low birthweight (lower panel) 1980-2004.



Gluckman, Hanson and Fukuoka *Lancet* 2007;369:1081-2

日本では、出生体重低下の持続で、身長体重が低下していくとの危機感



Dennis Normile

EPIDEMIOLOGY

Staying slim during pregnancy carries a price
 Japanese are shrinking as low birth weight rises; their health may be at risk as well

By Dennis Normile

Japan's obsession with slender women may harm unborn children and create long-term health problems for the Japanese population. Already a high proportion of Japanese women is starting pregnancy underweight, and many scientists have criticized the country's official guidelines for weight gain during pregnancy as too strict. Now, a survey shows many pregnant women strive to keep their weight gain below even those targets.

The impact could go far beyond weight, says personal epidemiologist Nobuo Morikawa of Japan's National Center for Child Health and Development in Tokyo, who led the new study. "Signs may experience an increased disease burden among adults, and there could be an impact on longevity," she says. People born small are more prone to diabetes and hypertension, says Peter Chalkman, an expert on the developmental origins of health and disease at the University of Auckland in New Zealand, who calls the situation "truly alarming." "We're tried very hard to convince Japan's manufacturers, clinicians and their spokespersons for Japan's Ministry of Health, Labor and Welfare that there are no plans to do so."

The shortening of the Japanese is stark, but unmistakable. An international study published in 2005 found that since the late 19th century, the average Japanese adult male height rose 14.5 centimeters, peaking at 174.5 centimeters for those born in 1970 and 1979. But by the 1996 birth cohort, that had dropped to 173.5 centimeters. Over the same period, average female height jumped 17 centimeters, topped out at 163.5 centimeters, then dropped by 0.5 centimeters. Some other countries have also experienced height declines, which the study notably linked to economic pressure, an influx of shorter immigrants, or—in the United States—dietary habits, which can impair growth both in the fetus and in newborn babies.

In Japan, experts say the evidence for a link with lower birth weights is strong, as the country recovered from World War II. The percentage of low-birth-weight babies—those weighing 2.5 kilograms or less at delivery—dropped from 22% in 1955 to 2.5% in 1970-79. As babies grew heavier, however, doctors worried about preterm babies, a complication that can put the lives of both mother and baby at risk. In the late 1970s, some Japanese obstetricians suggested a low-calorie diet could lower that risk, a view incorporated

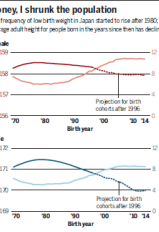
into 1980 guidelines from the Japan Society of Obstetrics and Gynecology. "Previously, mothers-to-be were told to 'eat for two'; now, the ideal is to 'give birth small but raise a big baby,'" says Hisako Fukuda, an obstetrician at Waseda University in Tokyo.

Health ministry recommendations issued in 1995 also reduced the average. The ministry adopted guidelines for U.S. women, produced by what was then called the U.S. Institute of Medicine (IOM), to the smaller and higher Japanese population, but in doing so made them considerably stricter. For underweight women—those with a body mass index (BMI) below 18.5—the guidelines sug-

gest a weight gain of 12.7 to 16.1 kilograms. Japan set the range at nine to 12 kilograms. Japanese women took the advice to heart, and the percentage of low-weight babies rose to 9.4% in 2004. That, this study found, led to a baby's height "to certainly establish and the weight" what we know from research links) did "warrant concern," Chalkman says. Morikawa has now confirmed that the desire to stay slim is contradicting the trend. Today, more than 30% of Japanese women in their 20s have BMIs of less than 18.5, compared with 12% of U.S. men and women aged 20 to 30. In a survey of 1085 pregnant women, 54% said their slight gestational weight gain was below the recommendations. Morikawa's team reports in a paper scheduled to appear online this week in *Scientific Reports*.

"The image Japanese mothers-to-be are striving for is the look of having a basketball in front of them while the rest of the body is slim," she says. The survey found that in addition to a quicker recovery of their pregnancy figures, women here for underweight gain did not reduce the risk of cesarean delivery or had no faster perinatal weight reduction. And the decline in birth weights means men born in 2004 will on average grow to be just 170 centimeters tall and women only 157.9 centimeters, Morikawa's team projects in a previous study.

Some think the culture is changing. The media are pushing more attention to the problem of low birth weights. Fukuda says, and dietitians and public-health groups "are re-examining their over undernourished young women." There seems to be a trend in the fashion magazines, going from slimmers to sportier," Morikawa adds. The latest government survey shows the percentage of underweight women in their 20s has dropped slightly since 2003. On the other hand, many slender pregnant women will just suffer on biological and share tips on managing weight gain. And most Japanese obstetricians are opposed to reducing the weight gain recommendations, says Shiroh Suzuki, an obstetrician at the Japanese Red Cross Kanakubo Maternity Hospital in Tokyo. Japan's fascination with being thin hasn't yet run its course, it



社会経済的な視点

低出生体重児の社会経済学的な調査

1) 学童期の成績低い

・**O-レベルテスト**: 英語・数学合計点25%以上低い)

(家族背景や環境を考慮しても有意)

(Currie et al. 1958)

2) 知的発達スコア (**Intellectual Development Score**) & 社会性発達スコア (**Social Development Score**) が低い

Breslau et al. 1994,

Brooks-Gunn, Klebanov, Duncan et al., 1996.

3) 成人期の賃金が低い。33歳での未就労率が高い。

(Currie et al. 1958)

Currie HEALTHY, WEALTHY, AND WISE:
SOCIOECONOMIC STATUS, POOR HEALTH IN CHILDHOOD, AND HUMAN CAPITAL
DEVELOPMENT (2009)

産後ケアの栄養学的あり方

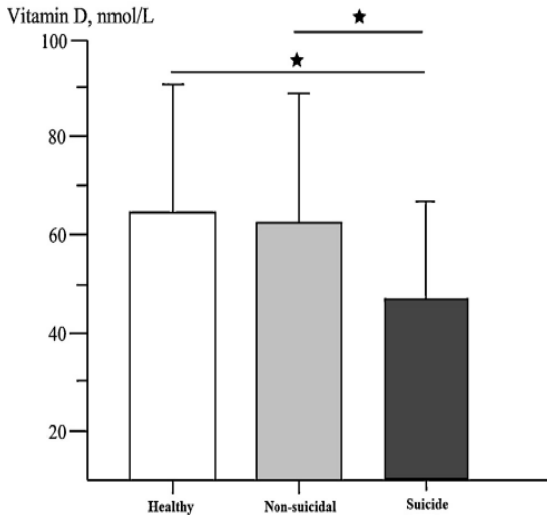
周産期・妊産婦死亡率（／出生10万人）

| | 周産期の自死率 | 妊産婦死亡率 |
|--------|---------|--------|
| 英国 | 2.3 | 3.7 |
| スウェーデン | 3.7 | 4.7 |
| 日本 | 8.7 | 3.96 |
| （東京都） | 8.7 | |

年間約80名の妊産婦・褥婦の自死
児虐待死58名（2011：心中は含まない）

政府統計e-Stat 及び東京都観察医務院・順天堂大学研究

自死行動者、鬱者、対照者の血中ビタミンD



[Grudet C., et al., Suicidal patients are deficient in vitamin D, associated with a pro-inflammatory status in the blood. Psychoneuroendocrinology. 2014;50:210-9.](#)

「当院で1人目を出産後に産後うつになられた方がいて、精神科医には「2人目はやめておいたほうがいい」とアドバイスをされるほど重症だったのですが、その方は2人目も希望されていました。セロトニン不足と考えられた事から栄養指導でたんぱく質をしっかり摂る様に勧め、サプリメントも提案しました。2人目の妊娠期では「前の妊娠中より調子がいい」と快調に過ごされて、**大きくて元気な赤ちゃん**を産みました。この一例からだけでいえる事ではありませんが妊娠出産の**メンタルケアに栄養が必要**である事は確かだと思います。」

産科婦人科館出張佐藤病院院長
佐藤雄一「第10回栄養と健康を考える有識者の会」日本栄養士会雑誌
2018.61:6-15

女性の“やせ”が及ぼす影響

1) 本人ライフコースへの影響

卵巣機能の低下
 月経不順、無月経(第一度、第二度)
 QOLの低下(中枢機能他)
 疾病リスクの増大

2) 次世代への影響

胎内低栄養のエピジェネティクス変化
 (世代を超えた疾病素因の伝達)
 次世代疾病リスク・医療費の増大

3) 社会への影響(少子高齢化より以上)

生産性・社会経済
 医療費、疾病構造

成人病(生活習慣病)胎児期発症説を知り、 育児する事でのリスク軽減 (DOHaD研究は介入法の開発へと進展)

1) 母乳哺育とスキンシップ

(母乳哺育が出来なくてもスキンシップが重要)

2) 規則正しいライフスタイルの確立

(時計遺伝子を考える:早寝早起き朝ごはん)

3) 運動習慣

4) 生後半年間の体重増加重要

(成長・発育チャートの利用)

5) 治療方法・薬剤の開発が進行中