

Endocrine disruption may have faded as an issue in Japan.

盛り上がり欠ける

日本での内分泌かく乱に関する議論

But it is more important than ever.

これまで以上に増大するその重要性

Pete Myers, Ph.D.,

ピート・マイヤーズ、Ph.D.

Environmental Health Sciences and Carnegie Mellon University

エンバイロメンタル・ヘルス・サイエンスズ／カーネギーメロン大学







カリフォルニア州パラダイス
2018年11月
死者88人

Paradise, California
November, 2018
88 dead



A silhouette of a city skyline, likely San Francisco, is visible against a hazy, orange-tinted sky at sunset or sunrise. The skyline includes several prominent buildings, such as the Transamerica Pyramid and the Transamerica Pyramid, and a lighthouse on the right. A single bird is seen in flight in the center of the sky.

妊娠中のビスフェノールAとフタル酸代謝物の尿内濃度測定と妊娠高血圧腎症リスク

Environ Health Perspect. 2016 Oct;124(10):1651-1655. Epub 2016 May 13.

Urinary Concentrations of Bisphenol A and Phthalate Metabolites Measured during Pregnancy and Risk of Preeclampsia.

Cantonwine DE¹, Meeker JD, Ferguson KK, Mukherjee B, Hauser R, McElrath TF.



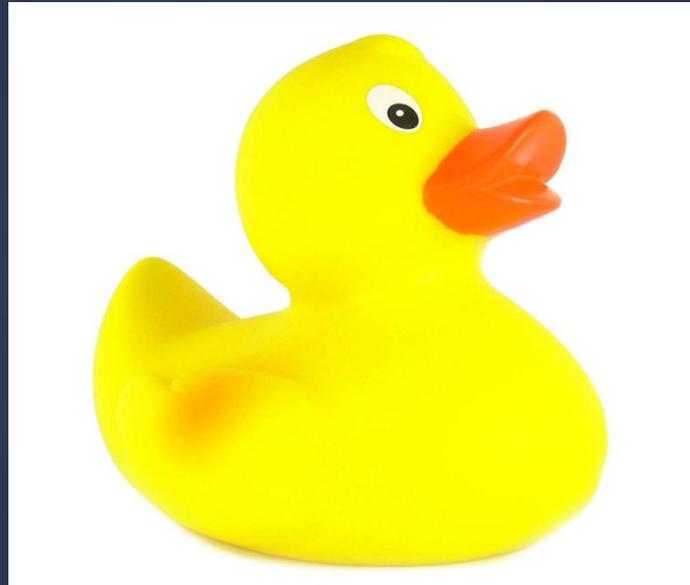
Living the plastic dream

プラスチックまみれの生活



70's – Breathing

70年代 - 呼吸



80's – Bathing

80年代 - 入浴



90's – Eating

90年代 - 食事

So here are our questions...

そこで湧いてくる疑問...

How did we get into this predicament?

いかにしてこうした状況に陥ったのか？

Why did we let EDC chemicals become so common?

なぜ内分泌かく乱化学物質（EDC）の蔓延が放置されたのか？

Is there a path forward?

この先に進むべき道はあるか？

Miracle material: Better living through chemistry

奇跡の素材：化学の力でより良い生活



© 1995 American Plastics Council



You could think of them as the sixth basic food group. Oh, you certainly wouldn't eat them, but plastic packaging does help pro-

help keep air out. While others let air in to help the food we eat stay fresher longer. Plastics also let you see what you're buying.

Plastics. An Important Part Of Your Healthy Diet.

tect our food in many ways. • To help lock in freshness, plastic wrap clings tightly to surfaces. To help lock out moisture, resealable containers provide a strong seal. And plastic wrap helps extend the shelf life of perishable produce, poultry, fish and meats. • To prevent spoilage and contamination, some varieties of plastics

taking the mystery out of shopping. All of which makes them versatile, durable, light-weight and shatter-resistant. • To learn more, call the American Plastics Council at 1.800.777.9500 for a free booklet. Plastics. One part of your diet you may never break.



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EDCs change how genes behave

遺伝子の挙動を変化させるEDC



Hormones guide gene expression

ホルモンが遺伝子発現を誘導



EDCs hack the system

EDCが遺伝子発現系を改変

Endocrine-Disrupting



THE
ENDOCRINE
SOCIETY®

Statement

Hormone-related cancers

ホルモン関連がん

ADHD

注意欠陥・多動性障害

Learning disabilities

学習障害

Pre-term birth

早産

Allergies
アレルギー

Infertility

不妊症

Endometriosis

子宮内膜症

Heart disease

心疾患

Diabetes

糖尿病

Autoimmunity

自己免疫

Degenerative diseases

変性疾患

Autism

自閉症

Fibroids
子宮筋腫

Obesity

肥満

Asthma

ぜんそく

polycystic ovaries

多嚢胞性卵巣

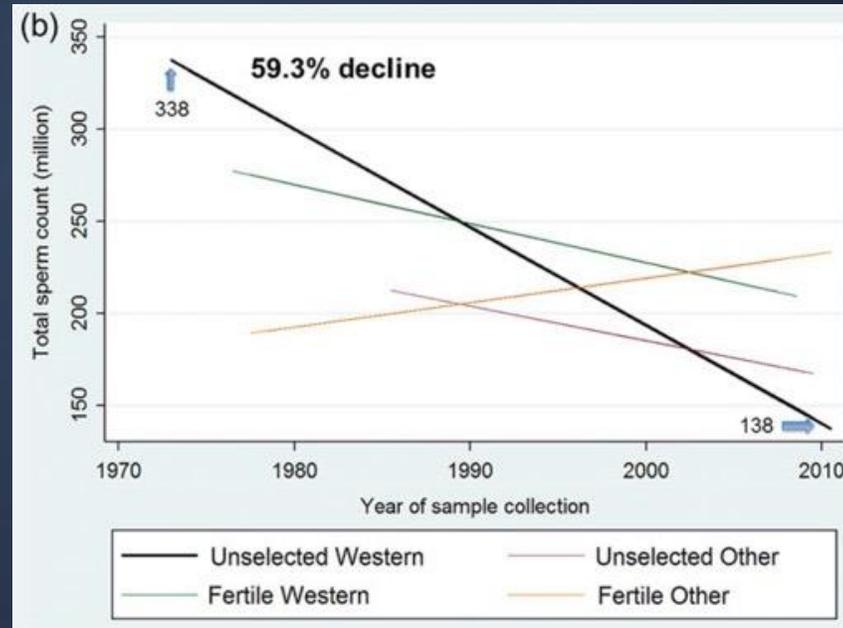
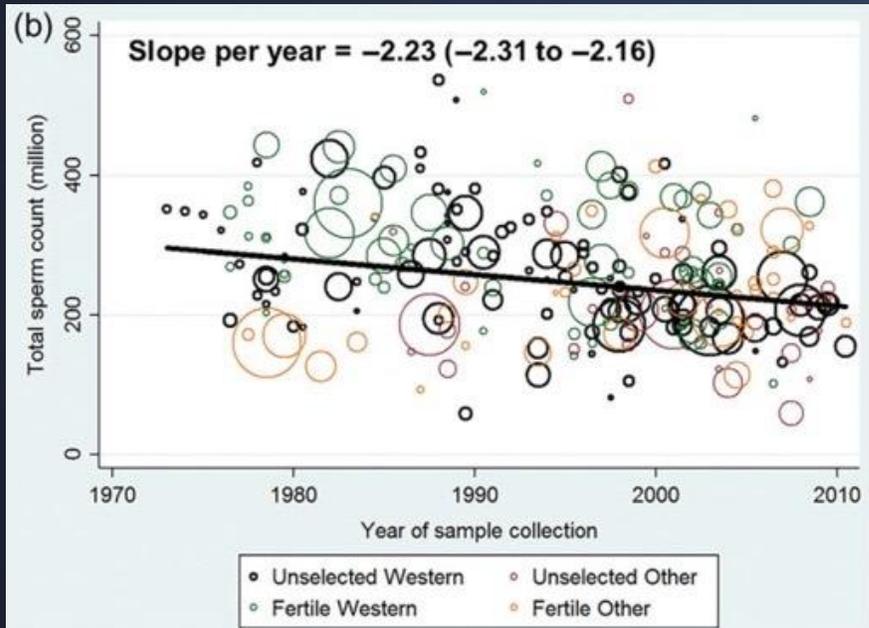


精子数の経時変動： 系統的レビューとメタ回帰分析

human
reproduction
update

Temporal trends in sperm count: a systematic review and meta-regression analysis

Hagai Levine^{1,2,*}, Niels Jørgensen³, Anderson Martino-Andrade^{2,4},
Jaime Mendiola⁵, Dan Weksler-Derri⁶, Irina Mindlis², Rachel Pinotti⁷,
and Shanna H. Swan²



Revolution in science

科学革命

1. Exposure to EDCs is ubiquitous

1. EDC曝露は遍在する

2. Low doses matter a lot

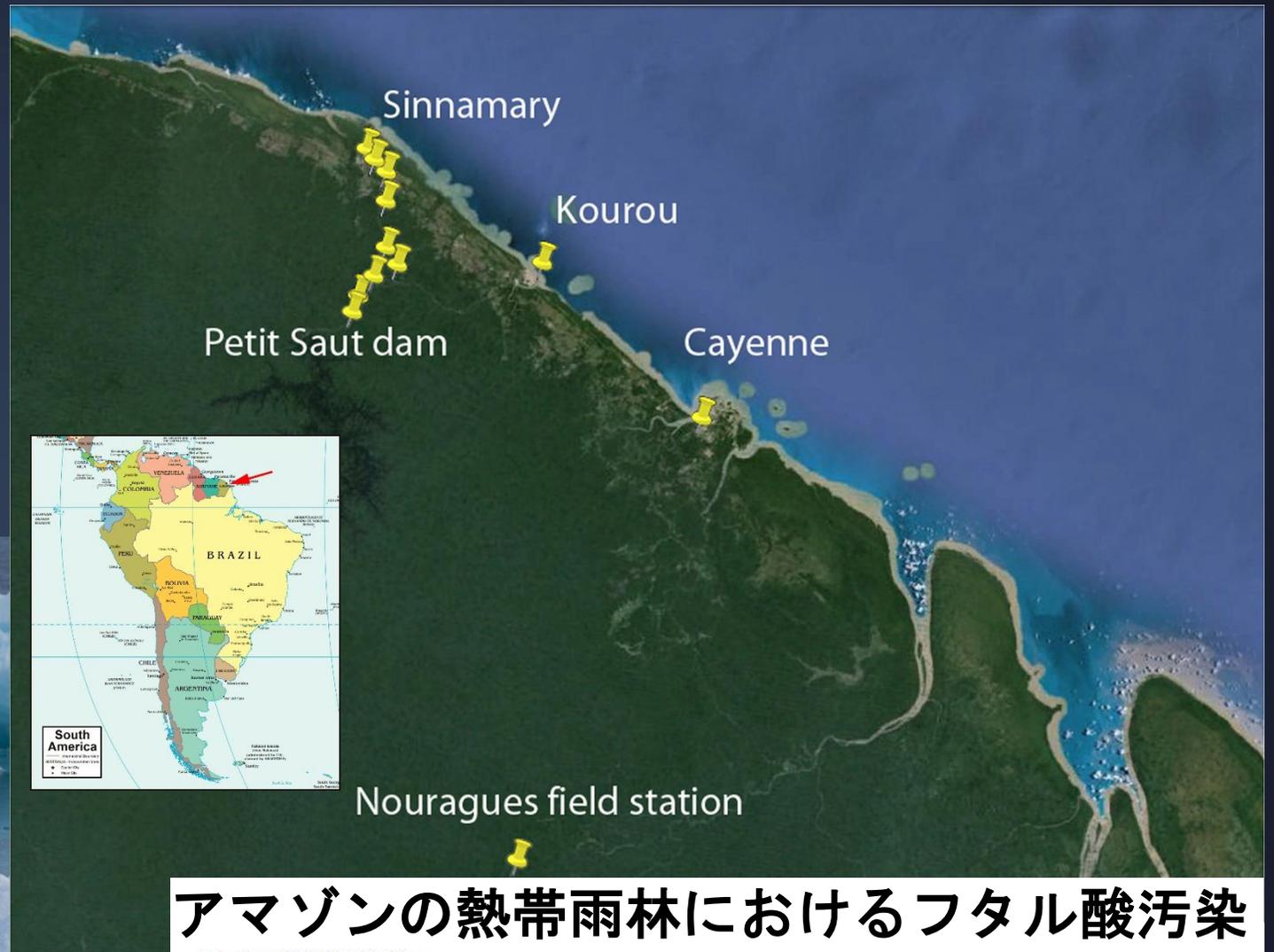
2. 少量でも影響は深刻

3. Events in the womb don't stay in the womb

3. 子宮内の事象は子宮に留まらない

4. Testing methods are deeply flawed

4. 試験方法に大きな不備



アマゾンの熱帯雨林におけるフタル酸汚染

Environ Sci Pollut Res
DOI 10.1007/s11356-016-7141-z

SHORT RESEARCH AND DISCUSSION ARTICLE

Phthalate pollution in an Amazonian rainforest

Alain Lenoir¹ · Raphaël Boulay¹ · Alain Dejean^{2,3} · Axel Touchard³ ·
Virginie Cuuillier-Hot⁴

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I began to have questions...

私は疑問を抱くようになった...

Are 'low doses' really low?

「低用量曝露」は本当に影響も少ないのか？

What's a part per billion?

何が10億分の1か？

How many molecules?

分子数は？

2.65 trillion

2兆6500億個





Perfluorinated compounds in artificial turf
人工芝に含まれる
有機フッ素化合物

有機フッ素化合物に起因する男性ホルモン活性の内分泌かく乱：臨床および実験からのエビデンス

Endocrine disruption of androgenic activity by perfluoroalkyl substances: clinical and experimental evidence

Andrea Di Nisio, Iva Sabovic, Umberto Valente, Simone Tescari, Maria Santa Rocca, Diego Guidolin, Stefano Dall'Acqua, Laura Acquasaliente, Nicola Pozzi, Mario Plebani, Andrea Garolla, Carlo Foresta

The Journal of Clinical Endocrinology & Metabolism

Endocrine Society

DOI: 10.1210/je.2018-01855

Perfluorinated compounds PFCs

有機フッ素化合物 (PFC)

1. Linked to many health outcomes

1. 多くの健康影響に関連

2. Incredibly persistent

2. 非常に分解しにくい

3. Widespread exposure

3. 曝露する可能性が至るところに存在

4. Most recent safe estimate: 0.1 ppt

4. 直近の安全推定値 : 0.1ppt

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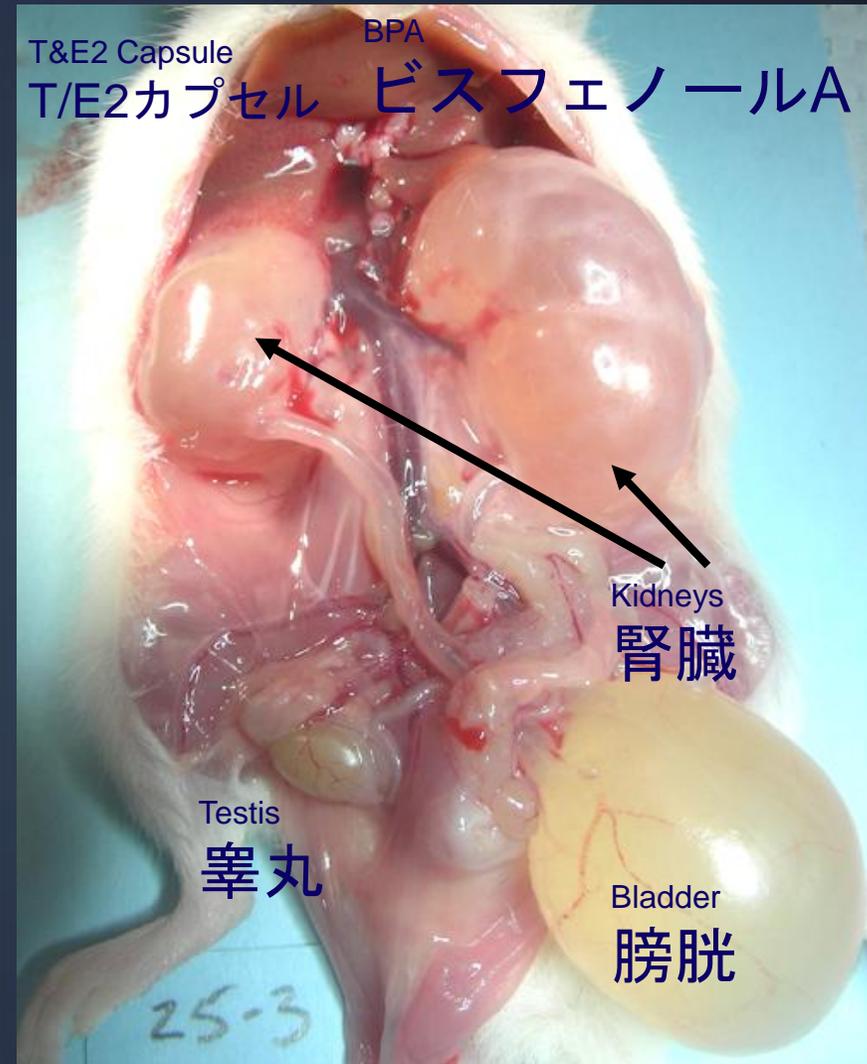
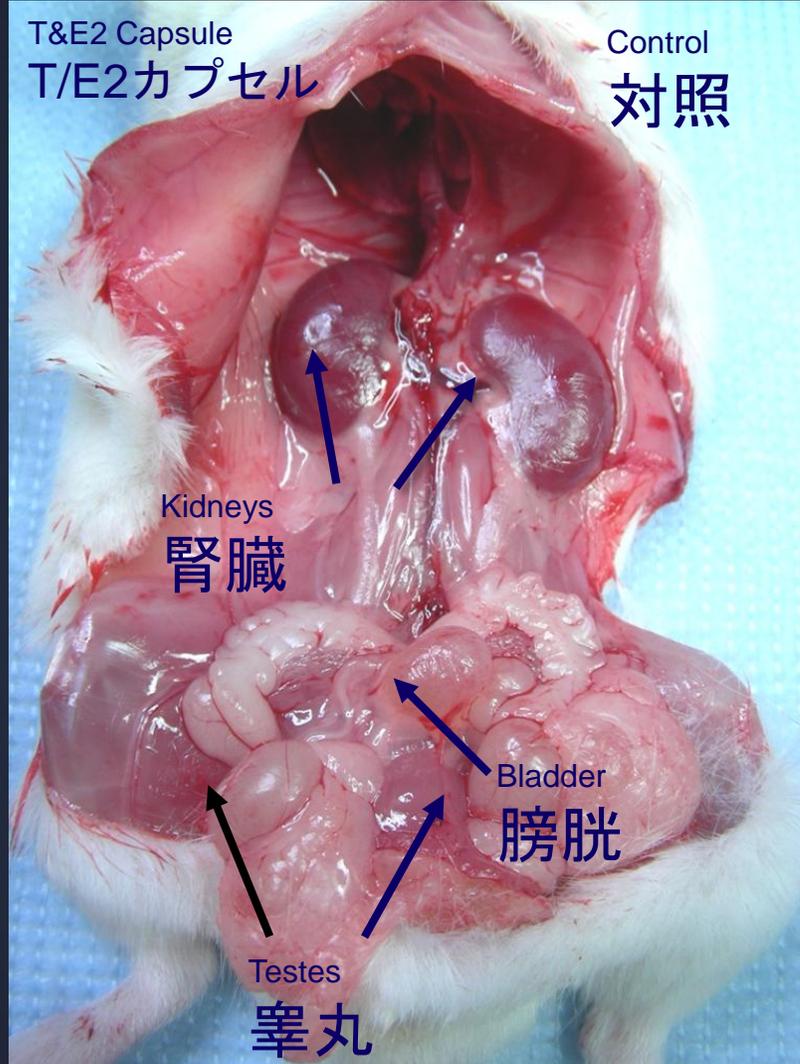
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ビスフェノールAの継世代効果は認識機能を低下させ、
マウスのシナプス後部の遺伝子発現を変化させる

Transgenerational Bisphenol A Causes Deficits in Social Recognition and Alters Postsynaptic Density Genes in Mice

Jennifer T Wolstenholme, Zuzana Drobná, Anne D Henriksen, Jessica A Goldsby, Rachel Stevenson, Joshua W Irvin, Jodi A Flaws, Emilie F Rissman ✉ Author Notes

Endocrinology, Volume 160, Issue 8, August 2019, Pages 1854–1867,
<https://doi.org/10.1210/en.2019-00196>

The current study using a transient exposure of gestating F0 generation female rats found negligible impacts of glyphosate on the directly exposed F0 generation, or F1 generation offspring pathology. In contrast, dramatic increases in pathologies in the F2 generation grand-offspring, and F3 transgenerational grand-offspring were observed. The transgenerational pathologies observed include prostate disease, obesity, kidney disease, ovarian disease, and parturition (birth) abnormalities.

OPEN

Received: 2 October 2018

Accepted: 9 April 2019

Published online: 23 April 2019

Assessment of Glyphosate Induced Epigenetic Transgenerational Inheritance of Pathologies and Sperm Epimutations: Generational Toxicology

Deepika Kubsad, Eric E. Nilsson, Stephanie E. King, Ingrid Sadler-Riggleman, Daniel Beck & Michael K. Skinner

除草剤グリホサートによる健康障害と精子のDNA上の化学的修飾異常（エピジェネティック変異）による世代を越えて継続する異常： 継世代毒性

世代を重ねて女性ホルモンかく乱物質を曝露することでオスのマウスで生殖細胞と生殖器官への影響が増大



Germline and reproductive tract effects intensify in male mice with successive generations of estrogenic exposure

Tegan S. Horan, Alyssa Marre, Terry Hassold, Crystal Lawson, Patricia A. Hunt*

School of Molecular Biosciences, Center for Reproductive Biology, Washington State University, Pullman, Washington, United States of America

PLoS Genet 13(7): e1006885. <https://doi.org/10.1371/journal.pgen.1006885>

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Painful realizations

痛ましい現実の認識

Most chemicals haven't been tested

ほとんどの化学物質が未試験

The tests used are flawed and outdated

使用される試験には不備があり時代遅れのもの

Core assumptions are wrong

中核をなす前提が間違っている

Analyses manipulated to hide problems

問題を隠すために分析結果が操作されている

09.18.19

Three-quarters of plastic products are toxic

プラスチック製品の4分の3は有害

ENVIRONMENTAL
Science & Technology

DOI: 10.1021/acs.est.9b02293

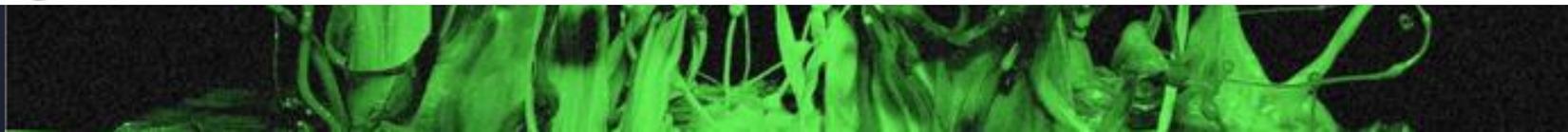
Article

プラスチック製品の細胞毒性と
化学組成の評価

pubs.acs.org/est

Benchmarking the in Vitro Toxicity and Chemical Composition of Plastic Consumer Products

Lisa Zimmermann,^{*,†} Georg Dierkes,[‡] Thomas A. Ternes,[‡] Carolin Völker,[§]
and Martin Wagner^{†,||}



Profoundly flawed assumptions

前提に大きな不備

The Paracelsus problem

パラケルススの問題

The cocktail effect

カクテル効果



ERAMUS DOCTOR

PARISELSVS

1 part per billion
10億分の1 (1ppb)



Same strain of mice 同じ血統のマウス
Same caloric intake 同じカロリー摂取量
Same activity levels 同じ活性レベル

Newbold *et al.* 2005, 2007

1 part per billion
10億分の1

What about 1000 ppb?

1000 ppbではどうか？



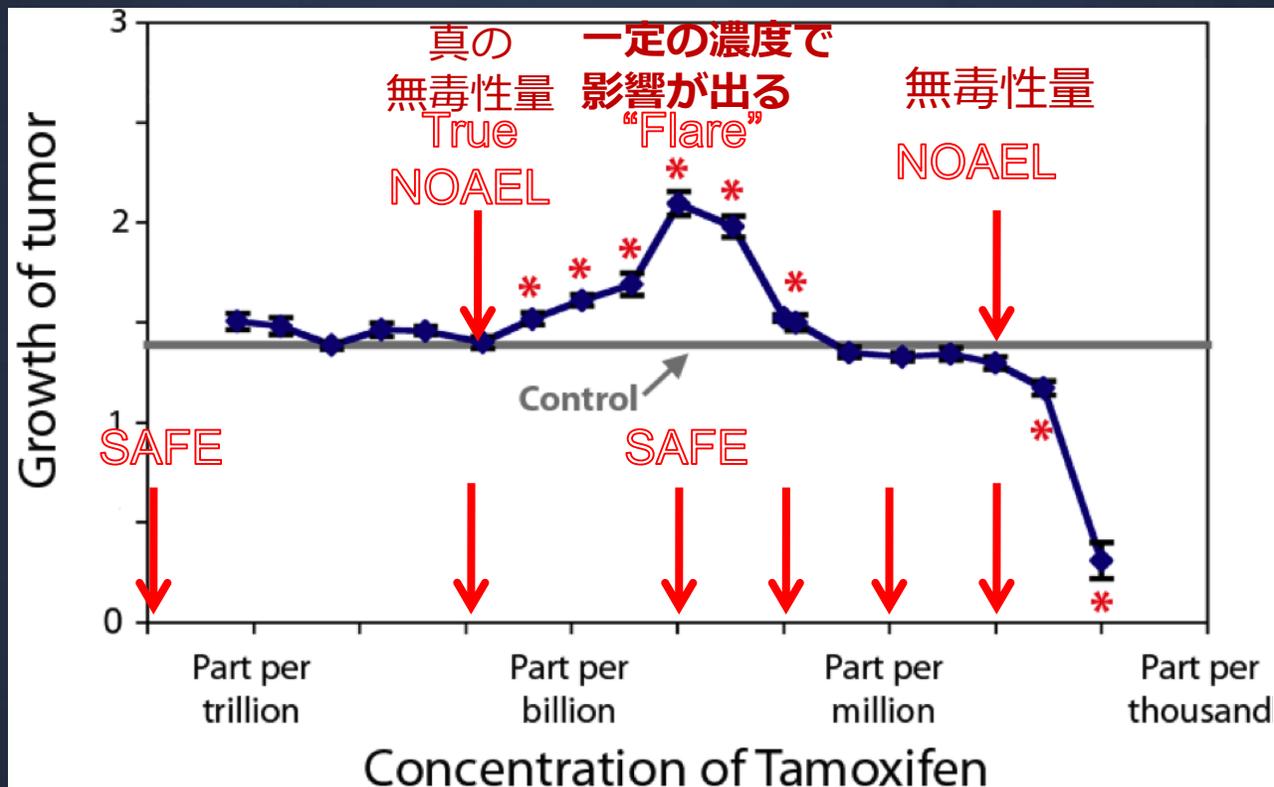
Same strain of mice 同じ血統のマウス

Same caloric intake 同じカロリー摂取量

Same activity levels 同じ活性レベル

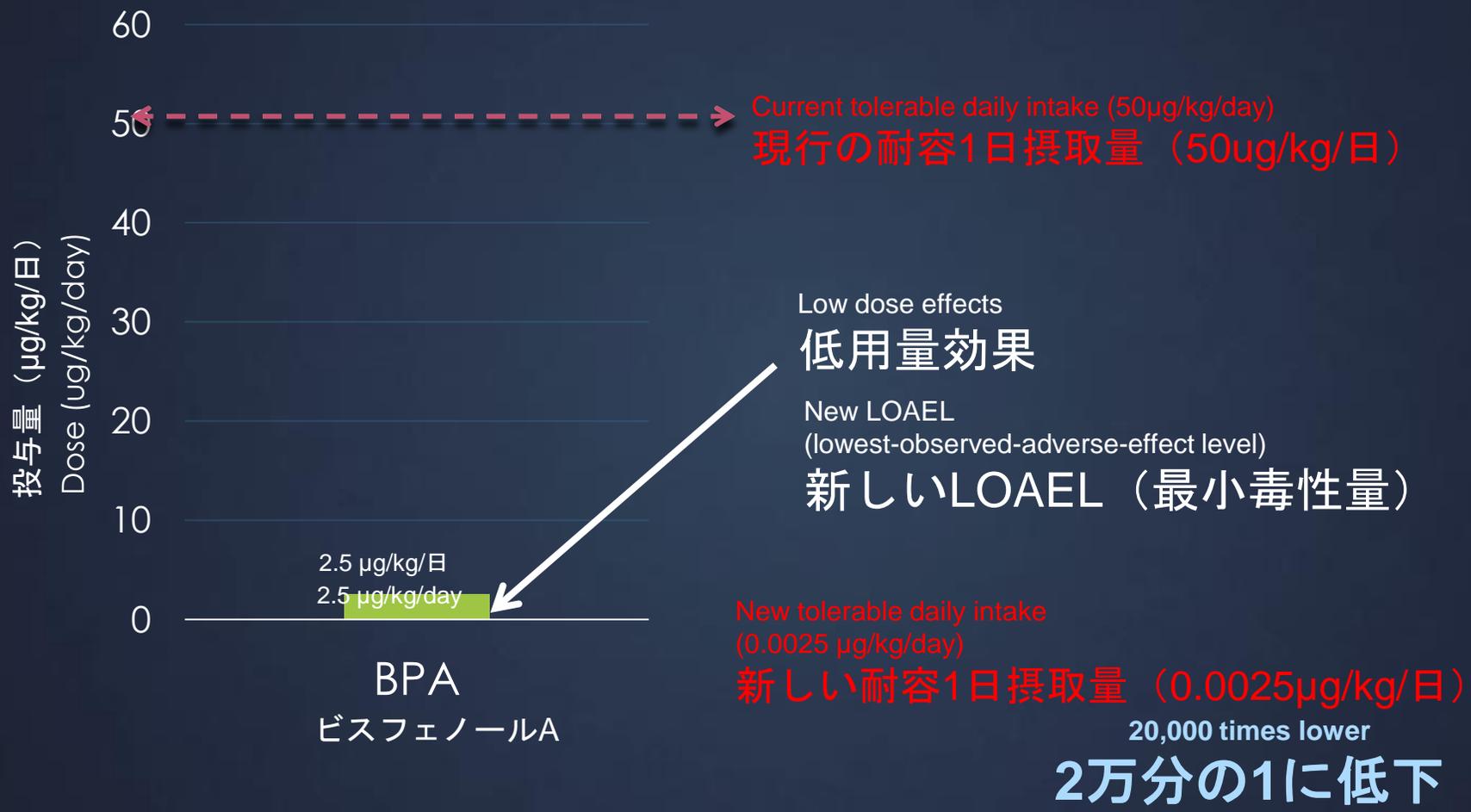
NON-MONOTONICITY OF TAMOXIFEN

タモキシフェンの濃度依存性にはならない影響



Welshons, in Vandenberg et al. 2012

タモキシフェン：女性ホルモンの作用を抑える抗女性ホルモン剤。乳がんの治療などに使用される。



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The cocktail effect

カクテル効果

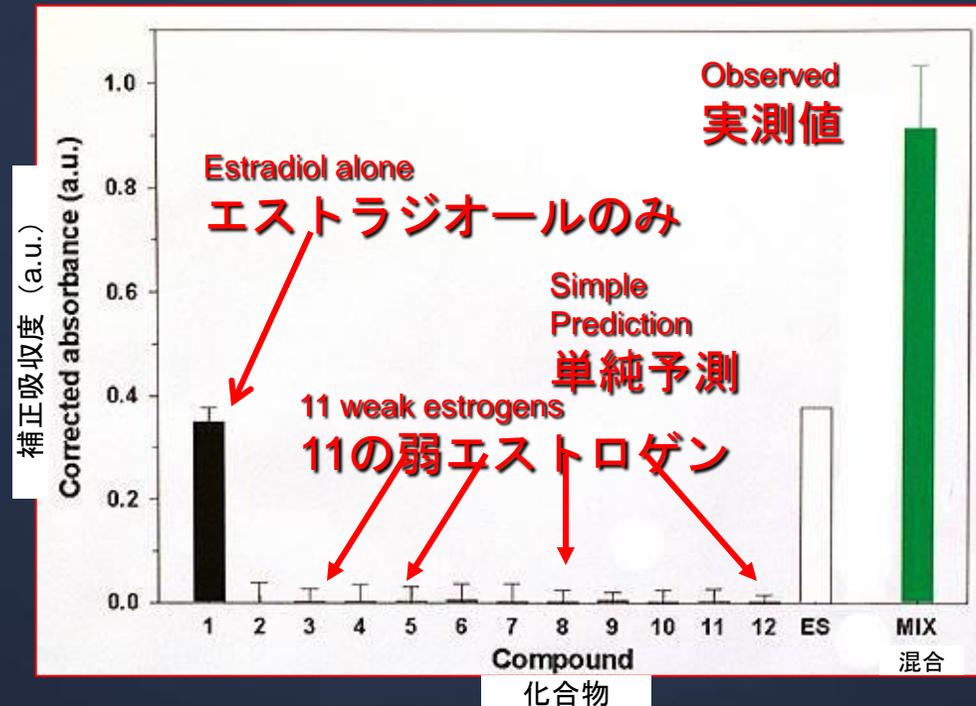


MIXTURES INTERACT

混合物は相互作用を起こす

US Centers for Disease Control data (NHANES)...

米国疾病対策センターのデータ（国民健康栄養調査）...



Rajapaske *et al.* 2002







Green Chemistry

Dynamic Article Links 

Cite this: DOI: 10.1039/c2gc35055f

次世代化学物質による内分泌かく乱のデザイン

PAPER

Designing endocrine disruption out of the next generation of chemicals†

T. T. Schug,^{*a} R. Abagyan,^b B. Blumberg,^c T. J. Collins,^d D. Crews,^e P. L. DeFur,^f S. M. Dickerson,^g
T. M. Edwards,^h A. C. Gore,ⁱ L. J. Guillette,^j T. Hayes,^k J. J. Heindel,^a A. Moores,^l H. B. Patisaul,^m T. L. Tal,ⁿ
K. A. Thayer,^o L. N. Vandenberg,^p J. C. Warner,^q C. S. Watson,^r F. S. vom Saal,^s R. T. Zoeller,^t
K. P. O'Brien^{*g} and J. P. Myers^{*u}

Received 12th January 2012, Accepted 4th September 2012

DOI: 10.1039/c2gc35055f

Redesign

デザイン変更

A new day

新時代

Reform

修正

Recharge

再投入

