생활 속 플라스틱

얼마나 되고, 어떤 영향을 주는가?

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About me

김선미

Environmental Health Scientist

2004년부터 4년간 여성환경연대 환경건강팀으로 활동, 2008년부터 2015년까지 환경독성학 연구실에서 석, 박사학위를 받고 연구교수로 재직 중. 무려 만12년이나 연구실 소속이었는데 그 중 1년 반은 세 아이를 낳으며 떠나 있었음(=그래도 만 10년간 무언가 꾸준히…). 3, 5, 9세 아이들을 키우며 환경보건문제의 중요성을 더 크게 느끼고 유해환경인자 노출과 건강과 관련, 위해성평가를 넘어서는 무언가를 활용하여 문제를 해결하는, 사회에 도움이 되는 연구자가 되는 것이 꿈.

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갑상선호르몬 교란

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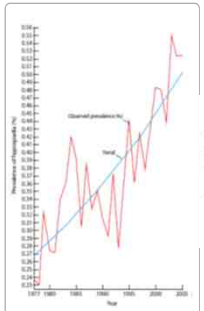
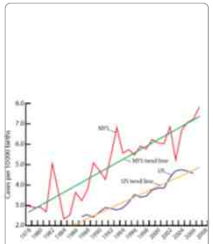
INTRODUCTION

현대사회 질병 급증, 원인이 무엇일까?

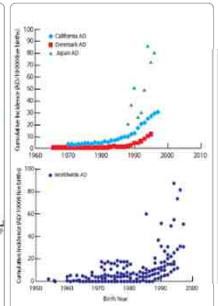
- **생식계이상, 갑상선호르몬이상, 당뇨, 비만, 만성신장질환 등...**



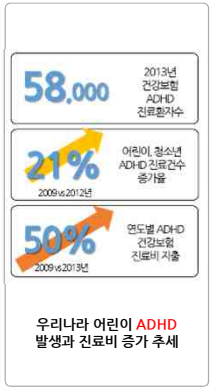
1977-2005년 덴마크 신생아요도하열(남아 성기기형) 발생추세



1978-2007년 미국, 뉴욕주의 신생아 갑상선저하증 발생추세

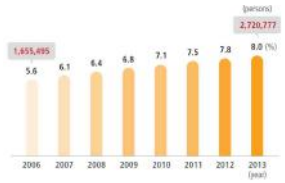


추적인구집단(코호트) 출생년도별 자폐증 발생추세



우리나라 어린이 ADHD 발생과 진료비 증가 추세

UNEP/WHO, 2012



당뇨병 유병률 추이(대한당뇨병학회 Fact Sheet 2015)

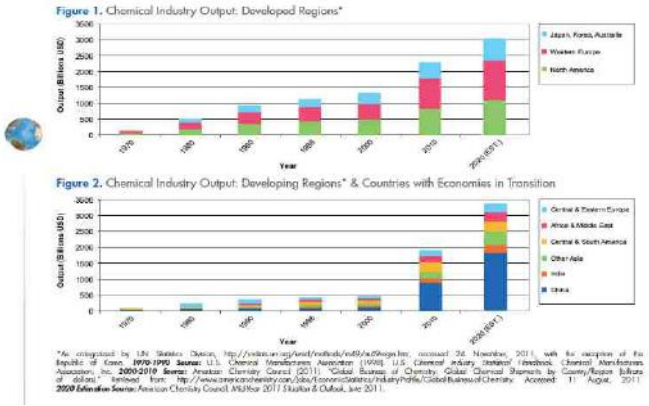
건보공단 DB 활용 여성질환 추세 및 분포(2015)

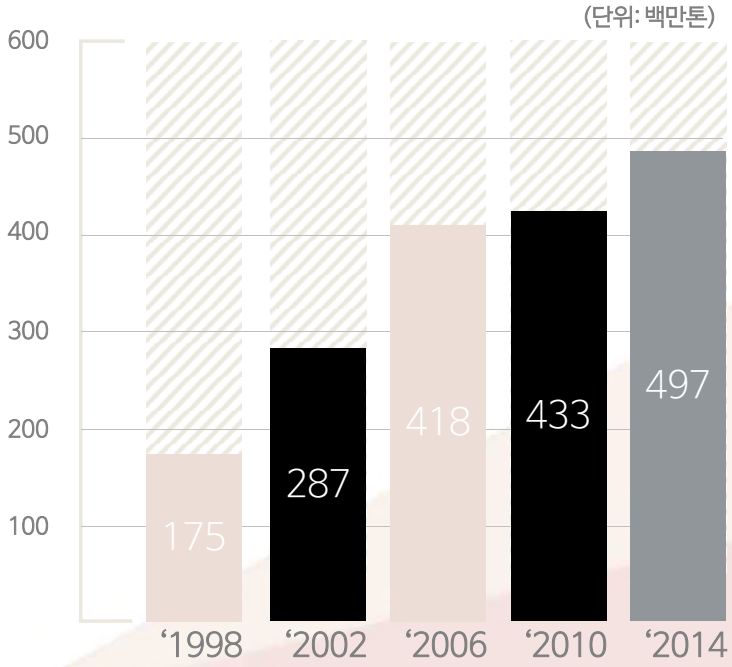
우리나라 만성신장질환 발생과 진료비 증가 추세

➡ **유전, 식이, 환경**

화학물질 사용량의 증가와 질병 급증

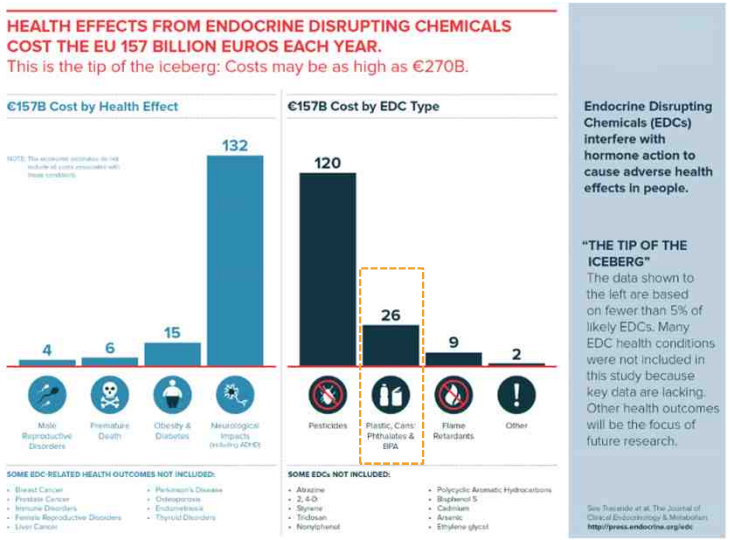
- 화학물질 유통량 지속 증가
- 전세계 화학물질 생산액 50년 동안 300배 증가

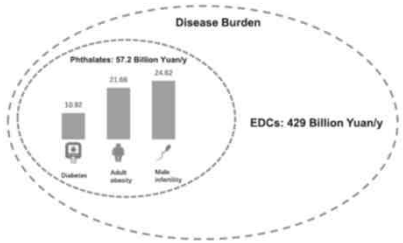




한국의 화학물질 유통량

EDCs 노출에 따르는 사회적 질병 부담





1570억 유로(약 207조 원)
GDP의 1% 수준

미국: 3천4백억 달러(약 395조 원)
GDP의 2.3% 수준

중국: 4천290억 위안(약 72조 62백억원)
GDP의 1.1% 수준

https://med.nyu.edu/departments-institutes/pediatrics/divisions/environmental-pediatrics/research/policy-initiatives

(Trasande 2015)

(Cao et al. 2019)

연구분야

▪ 환경보건학 (Environmental Health)

- 산업환경 및 생활환경에서 유발되는 각종 건강유해인자들의 파악과 관리
- 환경오염 저감, 환경유해인자가 인간의 건강에 미치는 영향을 최소한으로 만들고 환경문제 해결
- 복합학문, 사회참여적학문

연구분야

▪ 환경위해성평가

- 환경유해물질이 실제로 우리 몸(또는 생태계)에 나쁜 영향을 미칠 수 있는지 없는지 추정
- 환경위해성평가 분야의 대중적 이슈: 가습기살균제, 살충제 달걀, 생리대 안전성, 영수증 Bisphenols, 맥주 glyphosate….
- 위해성평가는 좋은 도구이나, 한계도 존재

환경독성학 Environmental toxicology	+	**노출과학** Exposure science
환경오염물질과 이화학적 요인들이 사람 및 생태계의 다양한 수용체에 미치는 독성 영향을 연구		다양한 환경유해인자가 사람에게 노출되는 정도를 정량적으로 추정하고 그 영향을 연구

▪ 환경역학(Environmental epidemiology)

- 환경유해인자 노출과 건강영향 간 상관관계와 인과관계 파악
- 위해성평가 결과와 다르게 부정적 건강영향 확인 가능

CHEMICALS in PLASTIC

일상 속 다양한 환경호르몬류

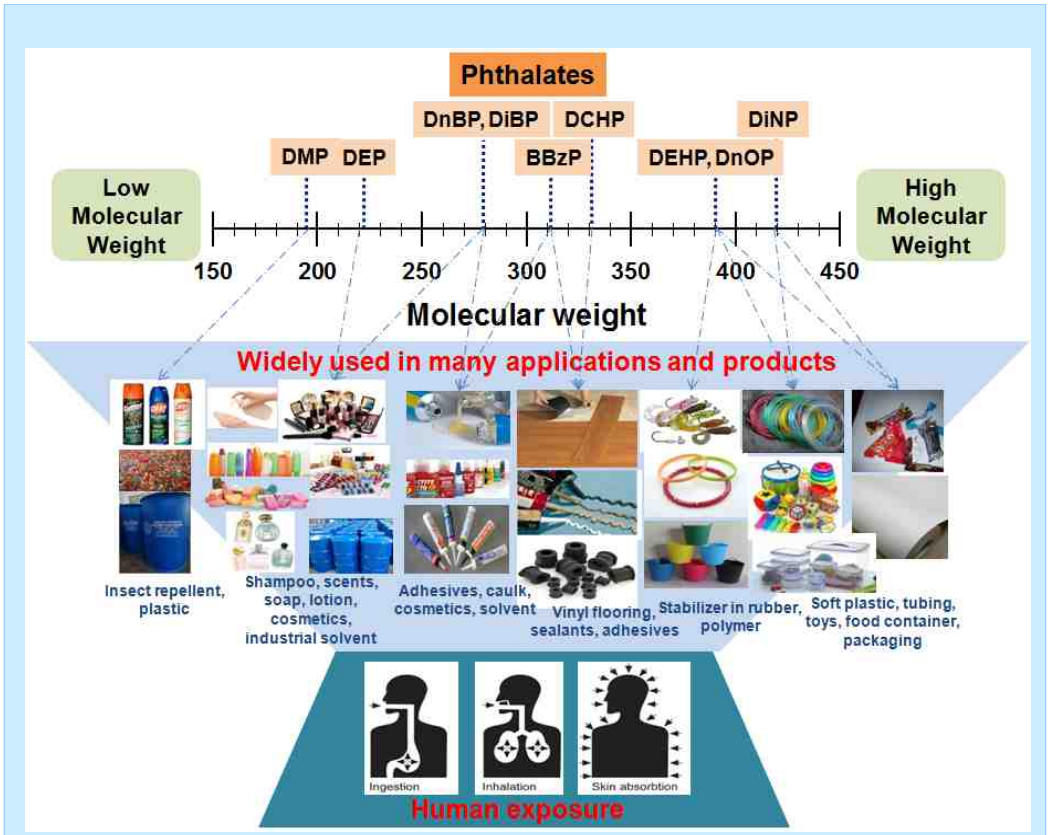
- **식이 및 식품포장재**
  –Bisphenol A, S, F, AF… ; Phthalates ; Perfluoroalkyl substances (PFASs)

- **화장품, 개인위생용품, 의약품 등** (Pharmaceuticals and personal care products: PPCPs)
  –Parabens; Triclosan; Benzophenones

- **일반 소비자제품, 생활화학제품** (청소용품, 건축자재, 의복, 의료기기, 장난감, 문구류 등)
  –Brominated and phosphorylated flame retardants ; Phthalates ; Perfluoroalkyl substances (PFASs)

- **살충제류**
  –Organophosphate pesticides ; Triazoles and other fungicides ; Pyrethroids ; Neonicotinoids

프탈레이트



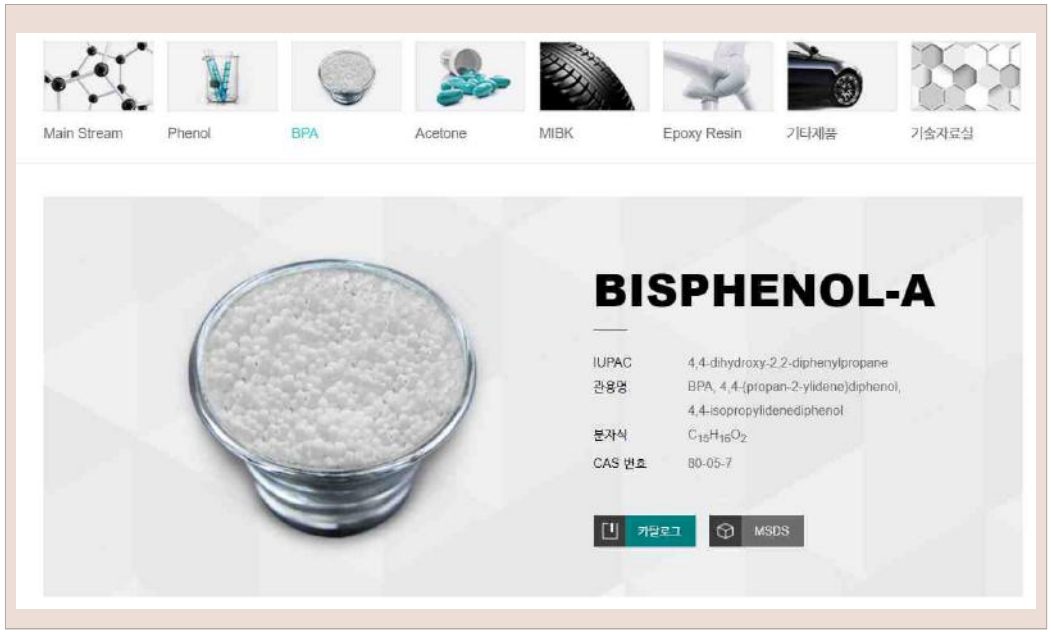
Phthalates

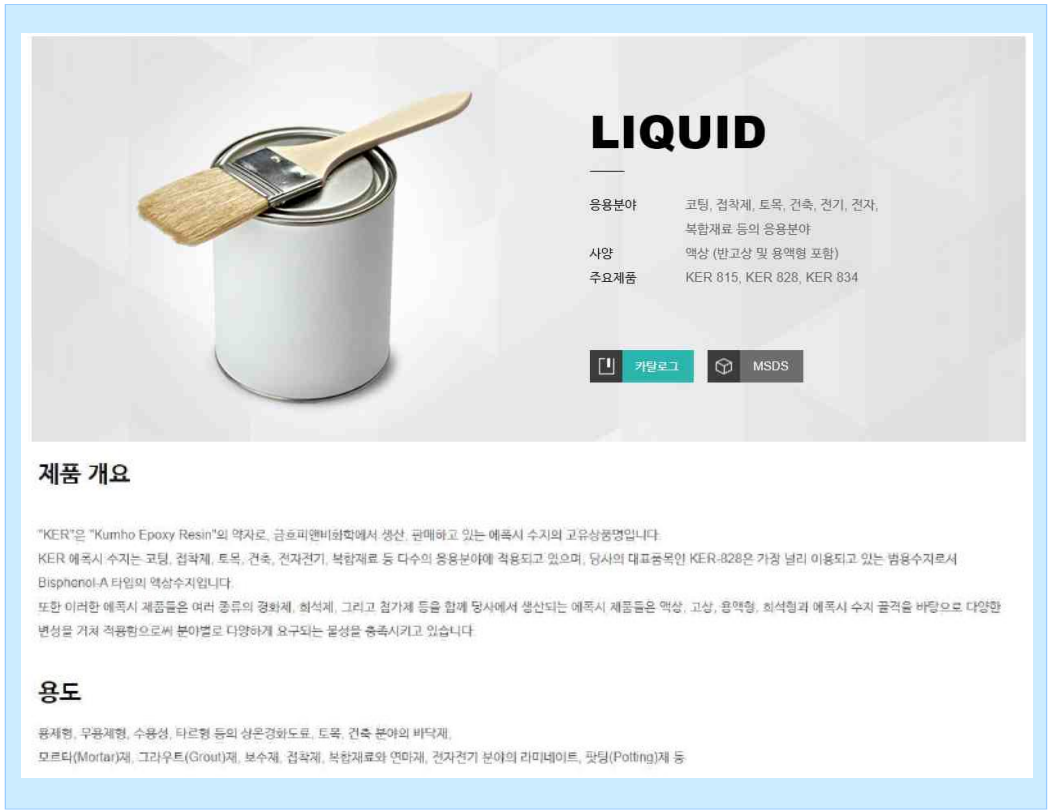
플라스틱 가소제, 용매 등으로 사용

다양한 종류와 물성 존재, 광범위 사용

대표적인 환경호르몬 - 성호르몬, 갑상선호르몬 교란 등등

비스페놀





BPA – 판매처

BPA, BPF 원료 및 합성수지

카탈로그 & MSDS - 인체, 생태독성 명시

Hazards classification information

- Reproductive toxicity	: Category 2
- Specific target organ toxicity (Single exposure)	: Category 3 (Respiratory tract irritation)

TOXICITY

환경호르몬의 특성

- **이화학적으로**
  - 생체에서 쉽게 배출되는 페놀류부터 잔류성과 축적성이 강한 유기물질까지 매우 다양함

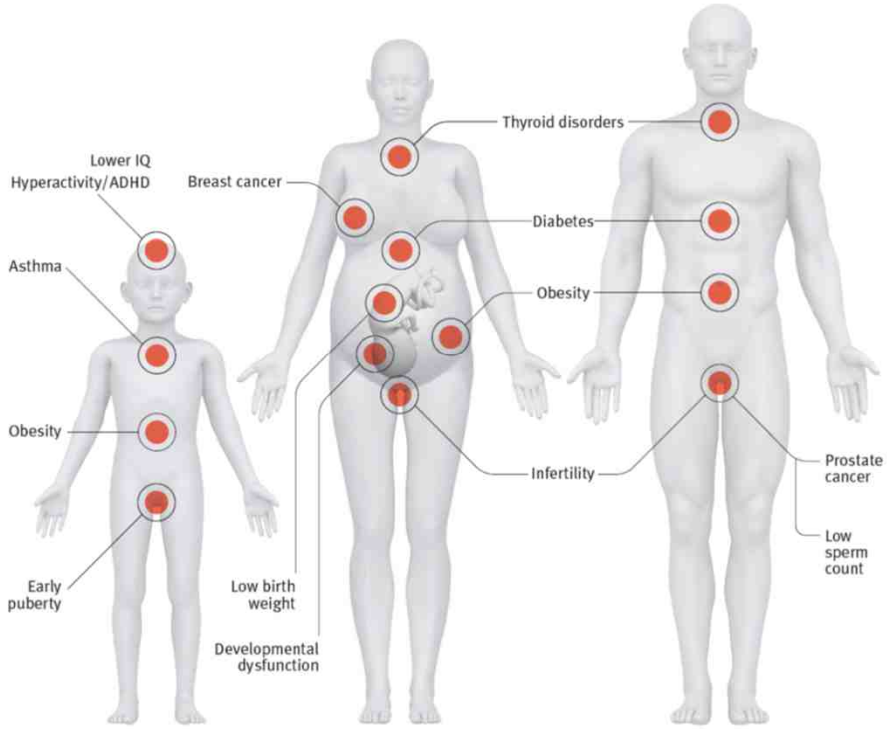
- **생물학적으로**
  - 호르몬과 비슷하게 작용하거나 호르몬 용량에 영향을 미쳐 저농도에서도 활성이 나타날 수 있음(저용량 효과)

- **노출시기에 따라**
  - 특정시기에 노출될 때 건강피해가 매우 심각하게 나타날 수 있음

Endocrine Disrupting Chemicals

Low Doses Matter

Everyday exposures to EDCs contribute to modern health epidemics.



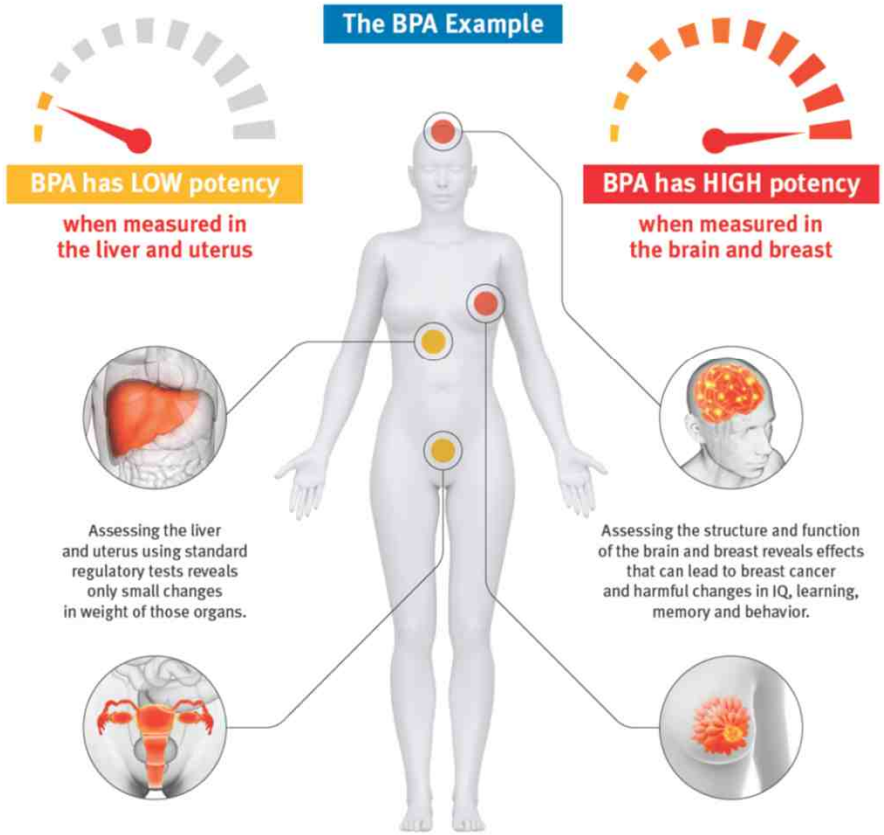
How are people exposed?

- Children's toys (phthalates)
- Plastic drinking bottles (BPA, BPS, BPF)
- Cleaning products (phthalates, triclosan)
- House dust (flame retardants, pesticides)
- Home furniture/electronics (flame retardants, PFAS)
- Building materials (flame retardants, phthalates, PFAS)
- Fragrances (phthalates)
- Food (pesticides like chlorpyrifos)
- Food packaging (BPA, PFAS, phthalates)
- Thermal cash register receipts (BPA, BPS)
- Drinking water (arsenic, lead, perchlorate)
- Personal care products (parabens, phthalates, triclosan)

Endocrine Disrupting Chemicals

Understanding Potency

An EDC does not have a single potency, so it should not be used for regulatory decisions.



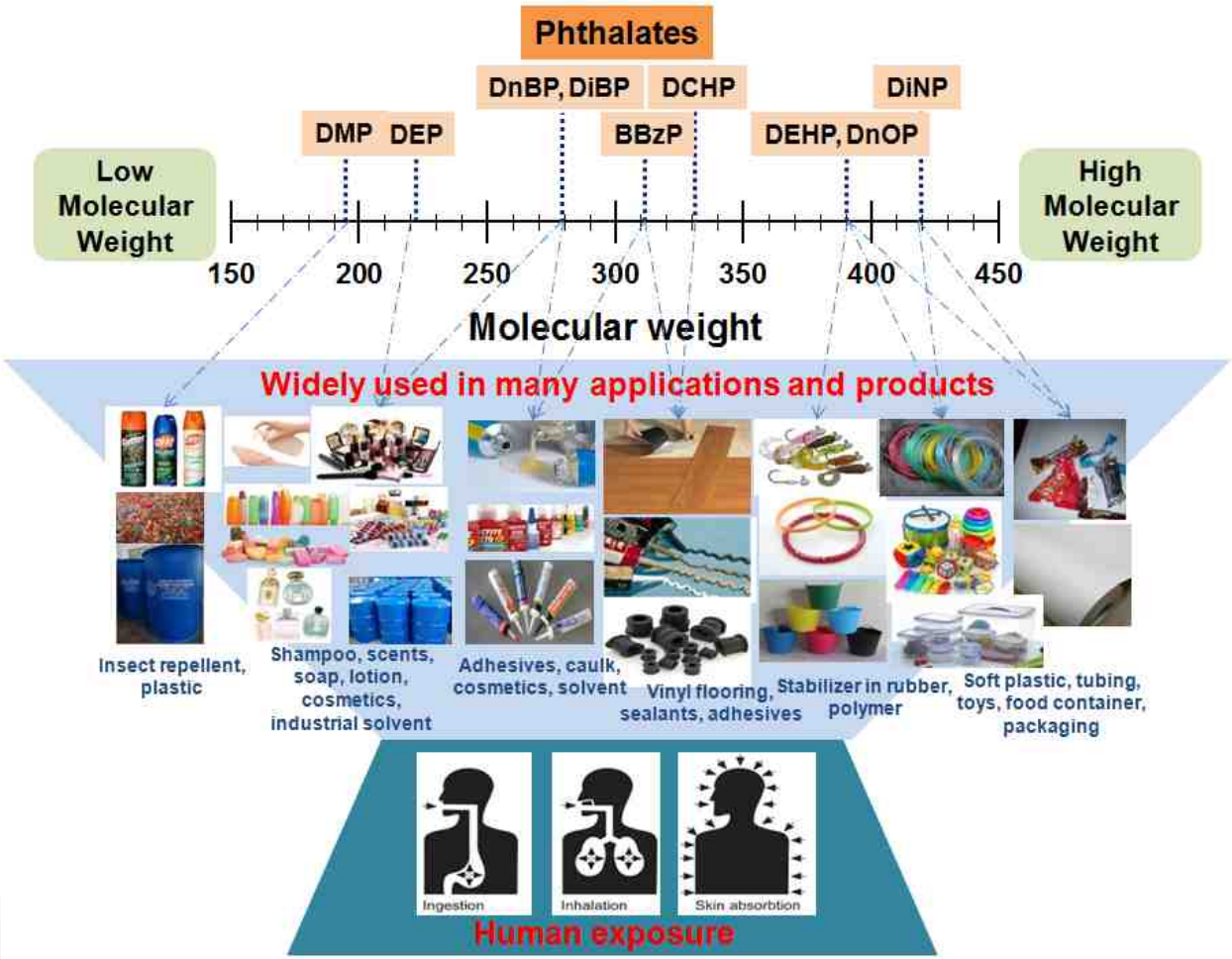
An EDC's potency depends on which organs you measure and how.

As measured in laboratory experiments

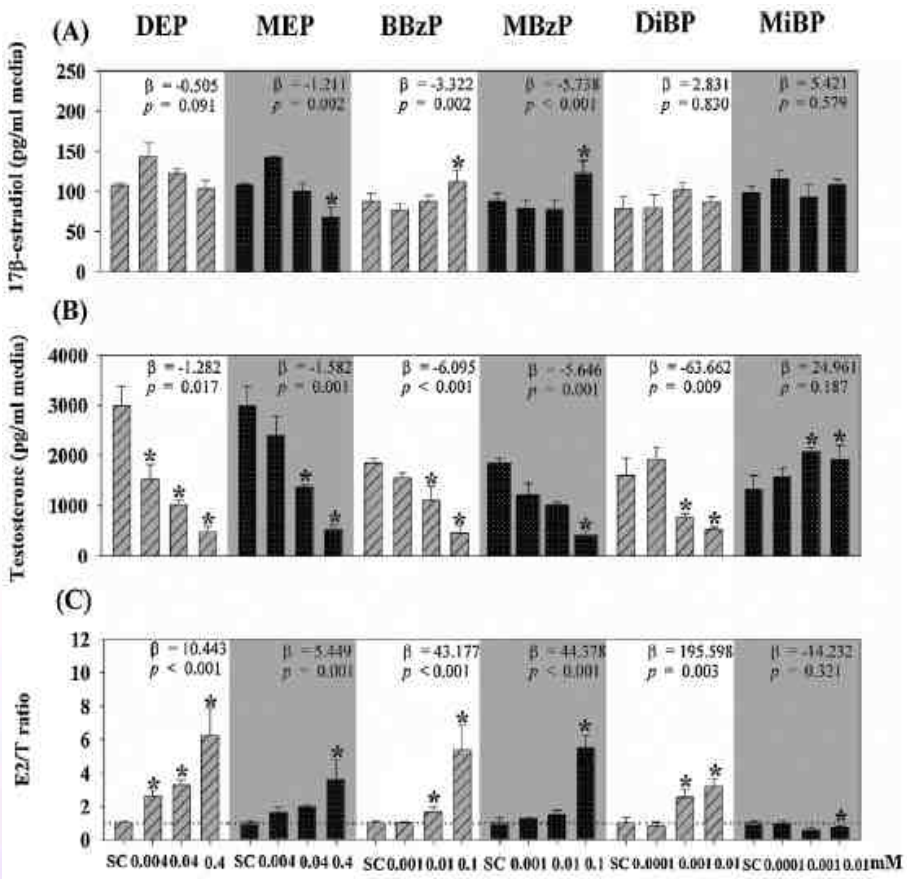
https://TEDX.org

프탈레이트

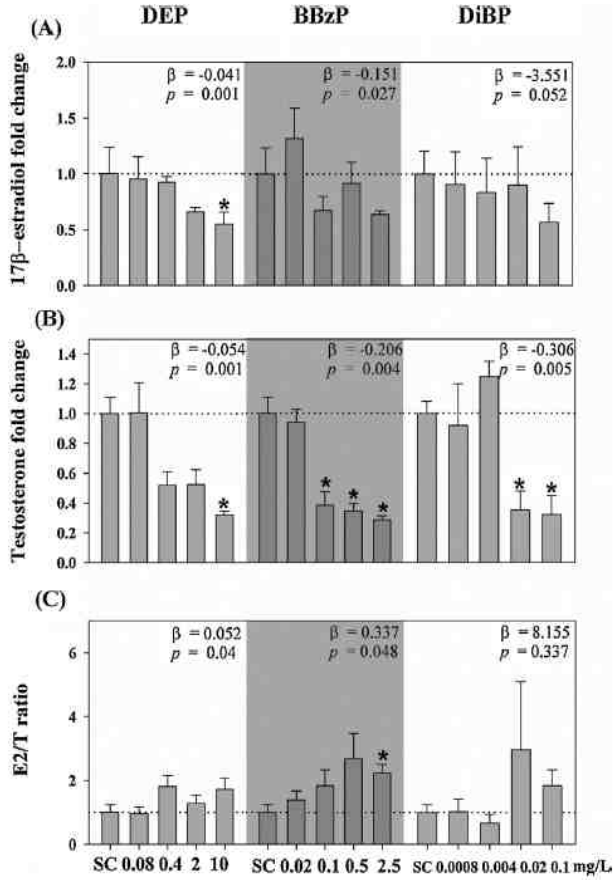
- **사용 용도**
  - 안정제(stabilizers), 분산제(dispersants), 윤활제(lubricants), 유화제(emulsifying agents) 등
  - 이화학적 특성과 사용용도 다양
- **주로 많이 사용된 프탈레이트류**
  - DEHP
  - BBzP
  - DnBP, DiBP
  - DEP



프탈레이트의 항안드로겐 작용 (anti-androgenicity)



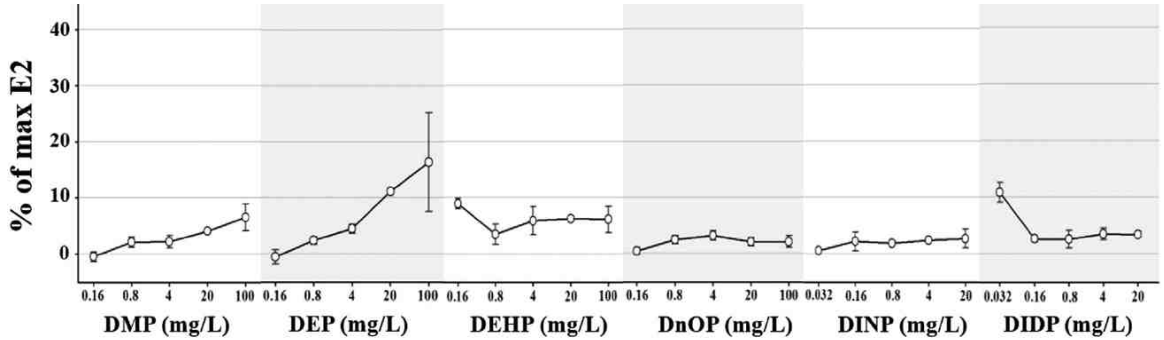
▪세포실험에서의 생식관련 호르몬생성과정 (steroidogenesis) 영향여부 확인

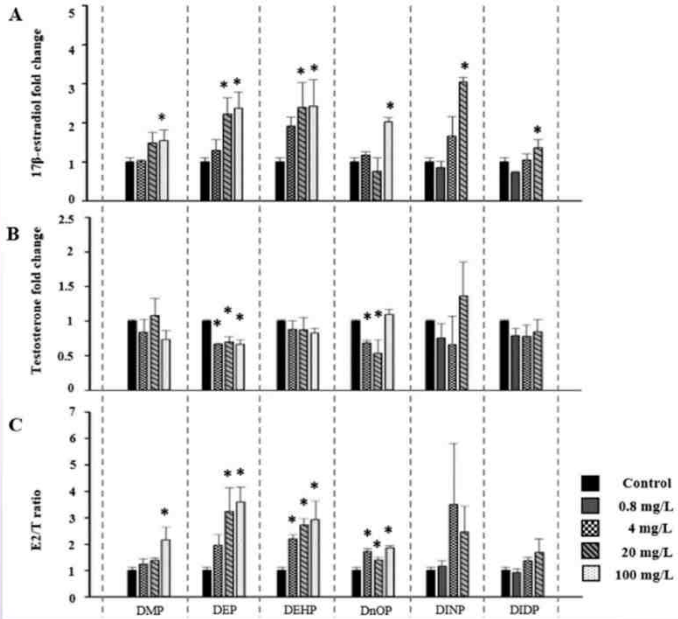


▪제브라피시 14일 노출에 의한 성호르몬 영향

(Sohn et al. 2016 Haz Mat)

프탈레이트의 항안드로겐 작용 (anti-androgenicity)





▪(위) 에스트로겐 수용체 (ER) 결합 통한 활성화 확인
- X축: log(실험농도), 단위: mg/L
- Y 축: %-E2max (ER binding affinity)

▪(왼) 생식관련 호르몬생성과정 (steroidogenesis) 영향여부 확인
- X축: 실험농도, 단위: mg/L
- Y 축: A: E2(에스트라디올) 증가율, B: 테스토스테론(T) 증가율,
  C: E2/T (estradiol/testosterone) ratio

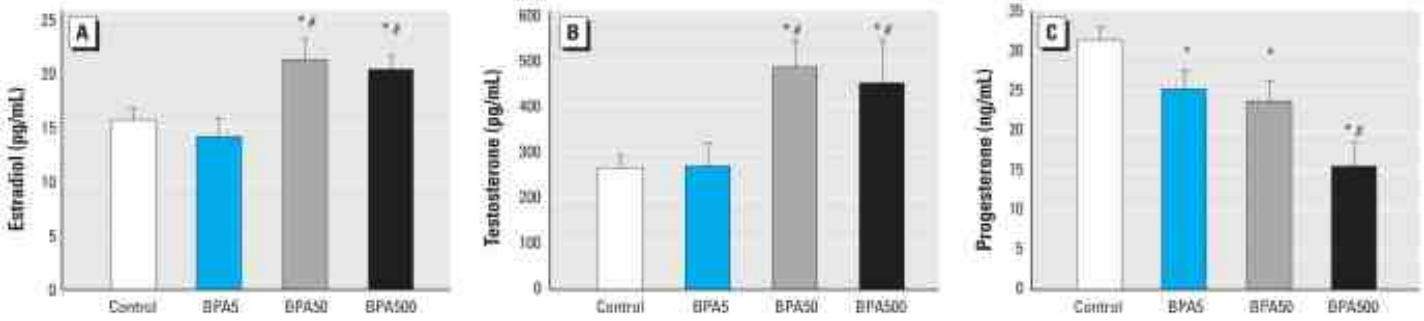
(Lee HJ et al. 2019 Env Res)

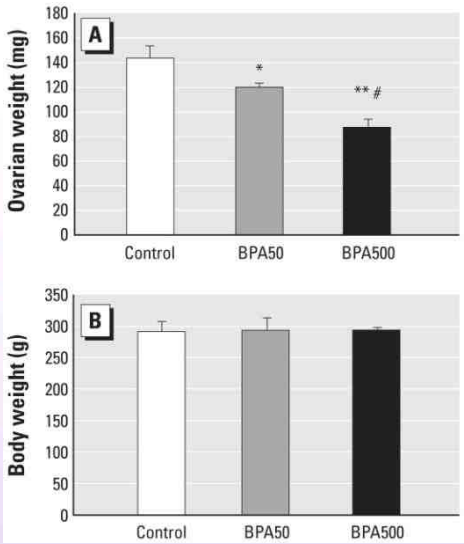
프탈레이트의 갑상선호르몬 교란

- **DEHP 노출과 갑상선 기능 관련 생물학적 실험(in vivo) 결과 요약**
  - 마우스 및 랫드에서 갑상선호르몬 T3, T4의 감소, TSH 변화 등 갑상선 기능 저하가 관찰(Ly et al. 2016, Ye et al. 2017, Liu et al. 2015, Sun et al. 2017, Tonk et al. 2012)
  - 랫드의 체중 대비 갑상선의 무게가 유의하게 증가(Dong et al. 2017)
  - 제브라피시에서는 갑상선호르몬 전환 및 운반에 관여하는 dio2와 ttr 유전자의 증가와 함께 갑상선호르몬 T3 및 T4의 농도가 유의하게 증가(Jia et al. 2016).

시험종 (발달단계, 성별)	노출경로	노출농도 (mg/kg)	노출기간	갑상선 관련 지표	주요결과	참고문헌
Mouse (8 weeks old, male)	Oral (gavage)	0.05, 0.5, 5, 50, 20	5 weeks	Serum total T3, T4, TSH	Decrease	Ly et al. (2016)
Rat (18 days old)	Oral (gavage)	250, 500, 750	30 days	Serum total T3, T4, free T3, T4	Decrease	Ye et al. (2017)
Rat (18 days old, male)	Oral (gavage)	250, 500, 750	30 days	Serum total T3, T4, free T3, T4	Decrease	Liu et al. (2015)
Rat (21 days old)	Oral (gavage)	5, 50, 500	28 days	Serum TRH, TSH, total T3, T4, free T3, T4	Increase	Sun et al. (2017)
Rat (7 weeks old)	Oral (gavage)	1, 3, 10, 30, 100, 300, 1000	Group 1: PND10-50, Group 2: PND50-90	Serum total T4	Decrease	Tonk et al. (2012)
Rat (4-6 weeks old)	Oral (gavage)	150, 300, 600	3-6 months	Thyroid/body weight(%)	3 m: increase, 6 m: no significant change	Dong et al. (2017)
Zebrafish (larvae, 168 hpf)	Waterborne	40, 100, 200, 400 μg/L	7 days	Whole body T3, T4, thyroid related gene expression (*ugt1ab, dio2, ttr*)	T3, T4: increase, *ugt1ab* gene: down-regulation, *dio2, ttr*: up-regulation	Jia et al. (2016)

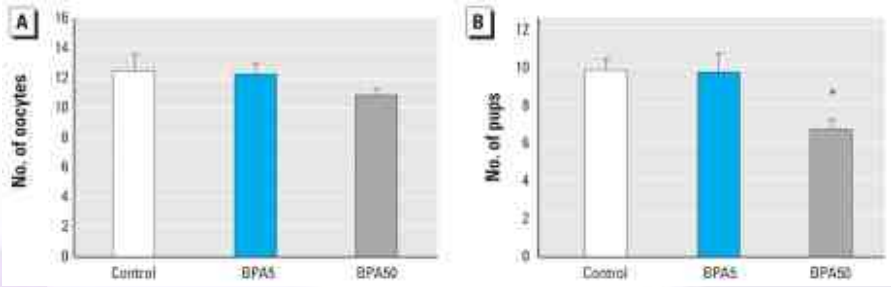
BPA의 항안드로겐 작용 (anti-androgenicity)

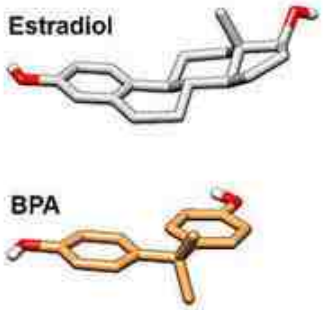




- (위) BPA 노출 후 성호르몬 농도 변화
- (왼) BPA 노출 후 난소 무게의 변화
- (아래) BPA 노출 후 난자 수, 산자수의 변화

(Fernandez et al., 2010)



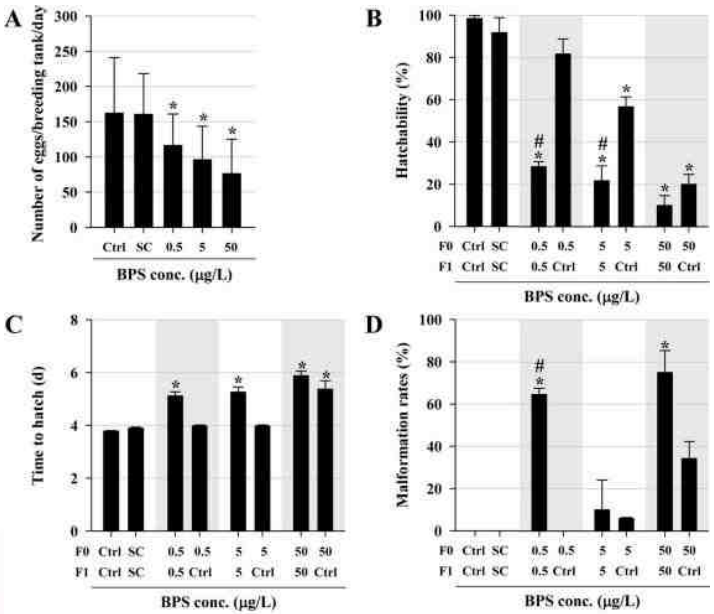


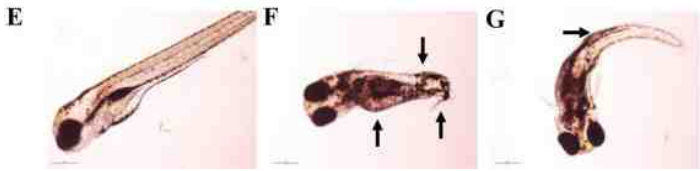
BPA의 갑상선호르몬 교란

- **BPA 노출과 갑상선 기능 관련 생물학적 실험(in vivo) 결과 요약**
  - 설치류 노출실험에서 갑상선호르몬 T3, T4 감소 및 TSH 감소/증가(Takagi et al. 2002, Viguie et al. 2013, Fernandez et al. 2018, Zoeller et al. 2015, Mahmoudi et al. 2018)
  - 체중대비 갑상선의 무게가 감소(Mahmoudi et al. 2018)
  - 제브라피시에서는 갑상선호르몬 관련 유전자가 유의하게 증가하여 갑상선호르몬 교란 가능성 (Genticore et al. 2013, Chan et al. 2012, Terrien et al. 2011).

시험종 (발달단계, 성별)	노출경로	노출농도 (mg/kg)	노출기간	갑상선 관련 지표	주요결과	참고문헌
Sheep (2-5 years old, female)	IV	5	GD28-end of pregnancy	Serum total T3, T4, free T4	Decrease	Viguie et al. (2013)
Rat (adult, female)	SC	5 µg, 50 µg, 500 µg/50 µL	PND1-PND10	Serum T4, TSH	T4: increase, TSH: decrease	Fernandez et al. (2018)
Rat (314±53 g, female)	Oral (diet)	1, 10, 50	GD2-GD20	Serum total T4, serum TSH	T4: increase, TSH: no significant change	Zoeller et al. (2015)
Rat (adult, 200g, female)	IM	250	20 days	Plasma TSH, free T3, T4, relative thyroid weight	Decrease	Mahmoudi et al. (2018)
Zebrafish (embryo)	Waterborne	10-8, 10-7, 10-6 M	24 hours	Thyroid related gene expression (tg, tsh, pas8, pax2a)	Up-regulation	Genticore et al. (2013)
Zebrafish (embryo-larvae)	Waterborne	0.80, 2.01, 4.02, 6.03 mg/L	96 hours	Thyroid related gene expression (nis, tg, tpo, trα, trβ, tshβ, ttr)	Up-regulation	Chan et al. (2012)
Zebrafish (embryo-larvae)	Waterborne	10-7, 5×10-7, 10-6, 5×10-6, 10-5 M	48 hours	Thyroid related gene expression (trα, trβ, tsh, mr, gr)	Up-regulation	Terrien et al (2011)

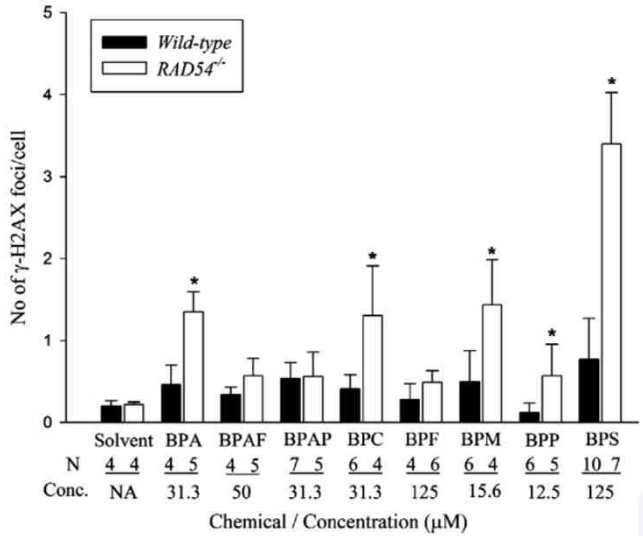
BPA 대체물질





- (위, 왼쪽) BPS 노출된 제브라피시에서의 생식지표, 기형여부
- (오른쪽) BPA 대체물질의 세포 유전독성 실험 결과

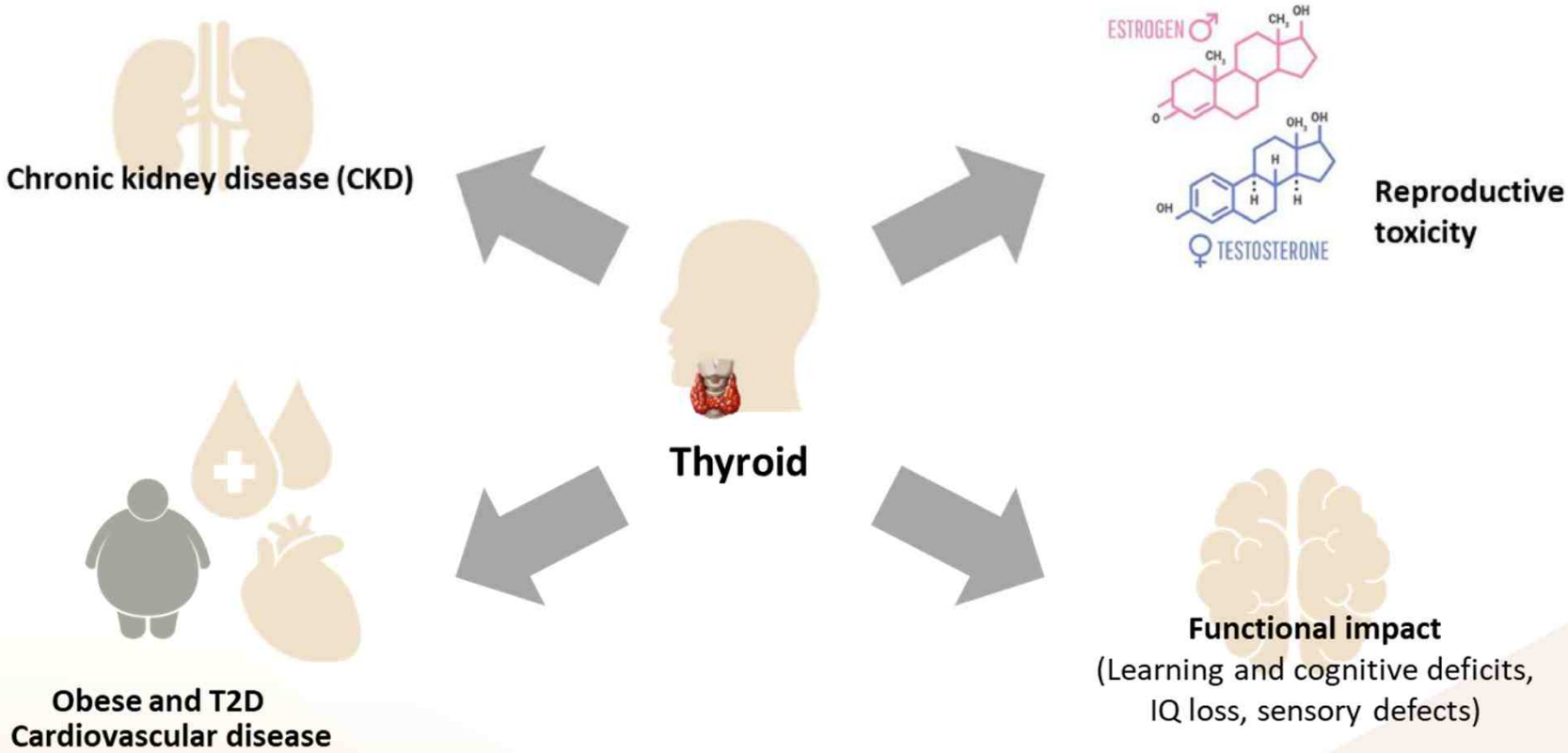
(Ji et al., 2012; Lee et al., 2016)



	BPA	BPAF	BPAP	BPC
	2,2-bis-(4-hydroxyphenyl) propane	4,4'-(Hexafluoro isopropylidene)diphenol	4,4'-(1-Phenylethylidene) bisphenol	2,2-Bis(4-hydroxy-3-methylphenyl)propane
Formula	$(CH_3)_2C(C_6H_4OH)_2$	$(CF_3)_2C(C_6H_4OH)_2$	$CH_3C(C_6H_5)(C_6H_4OH)_2$	$(CH_3)_2C[C_6H_3(CH_3)OH]_2$
CAS RN	80-05-7	1478-61-1	1571-75-1	79-97-0
MW	228.29	336.23	290.36	256.34
Purity (%)	≥99	97	99	97

	BPF	BPM	BPP	BPS
	Bis(4-hydroxyphenyl) Methane	4,4'-(1,3-Phenylene diisopropylidene)bisphenol	4,4'-(1,4-Phenylene diisopropylidene)bisphenol	4,4'-Sulfonyldiphenol
Formula	$CH_2(C_6H_4OH)_2$	$C_6H_4[C(CH_3)_2C_6H_4OH]_2$	$C_6H_4[C(CH_3)_2C_6H_4OH]_2$	$O_2S(C_6H_4OH)_2$
CAS RN	620-92-8	13595-25-0	2167-51-3	80-09-1
MW	200.23	346.46	346.46	250.27
Purity (%)	98	99	99	98

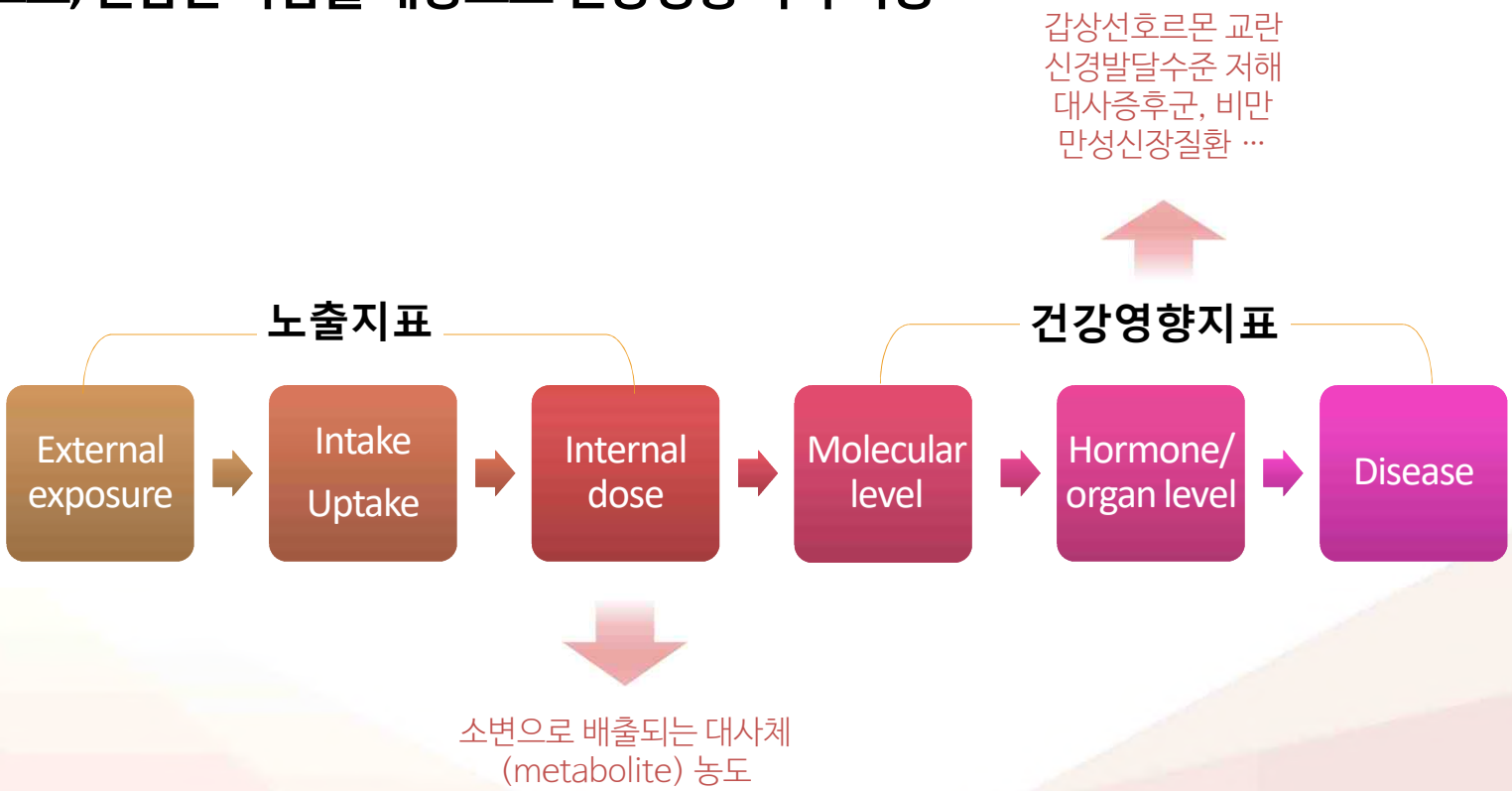
EDCs의 건강영향 – 인구집단 연구



EDC's Coordinated attack (Razvi et al. 2018; Mughal et al. 2018; Rhee 2016; Selva and Hammond 2009)

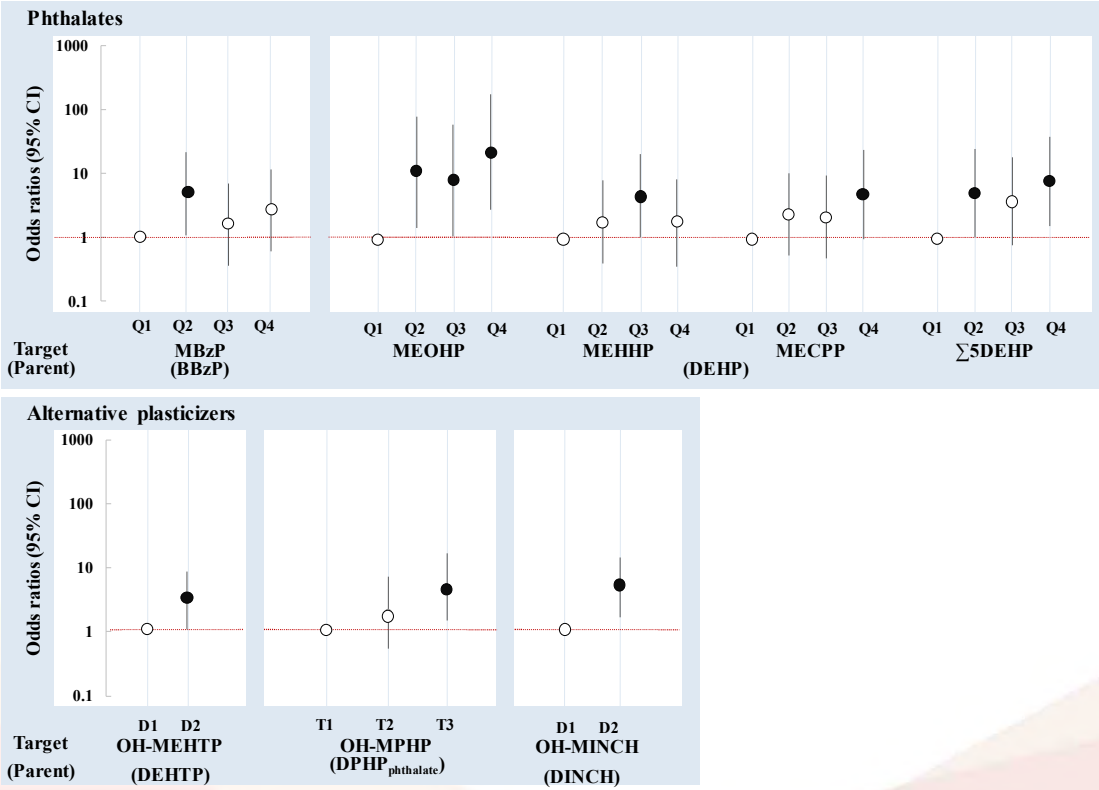
EDCs의 건강영향 – 인구집단 연구

- 환경역학연구를 통해
- 현실적으로, 민감한 사람들 대상으로 건강영향 파악 가능



여성성질환

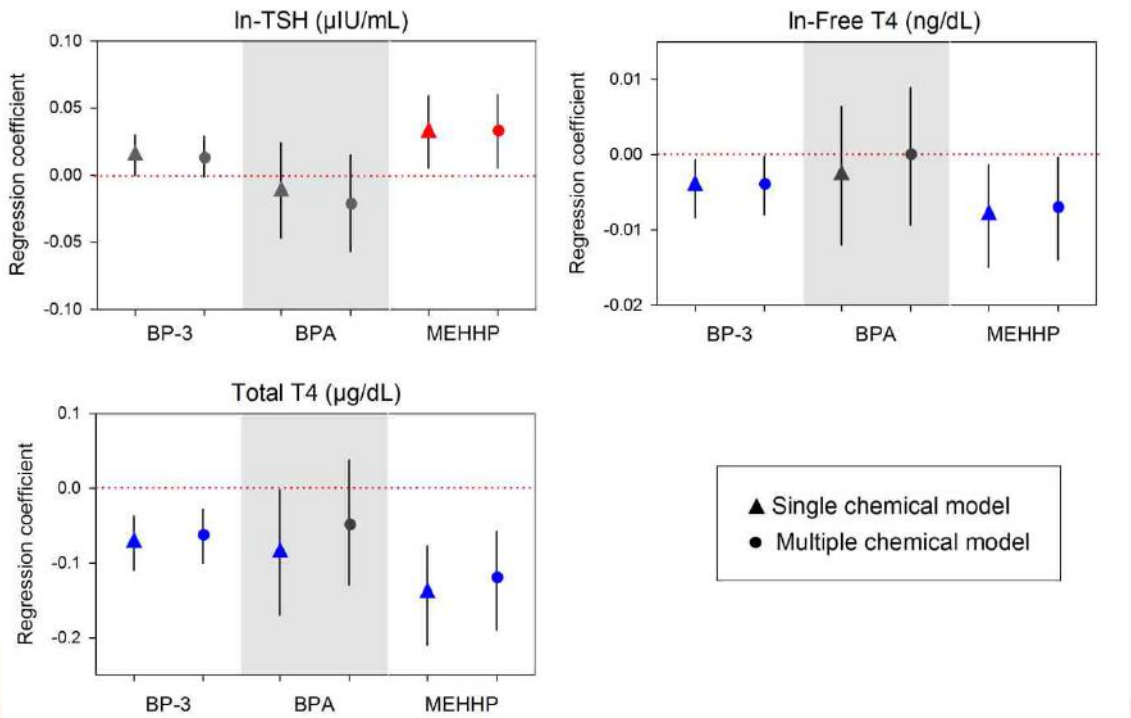
- **phthalate and alternative plasticizers in women and its association with uterine leiomyoma (n=111)**



(Lee G et al. In revision)

Thyroid hormone - related

- **Benzophenone, phthalate, and BPA in US general population (n=1,829)**

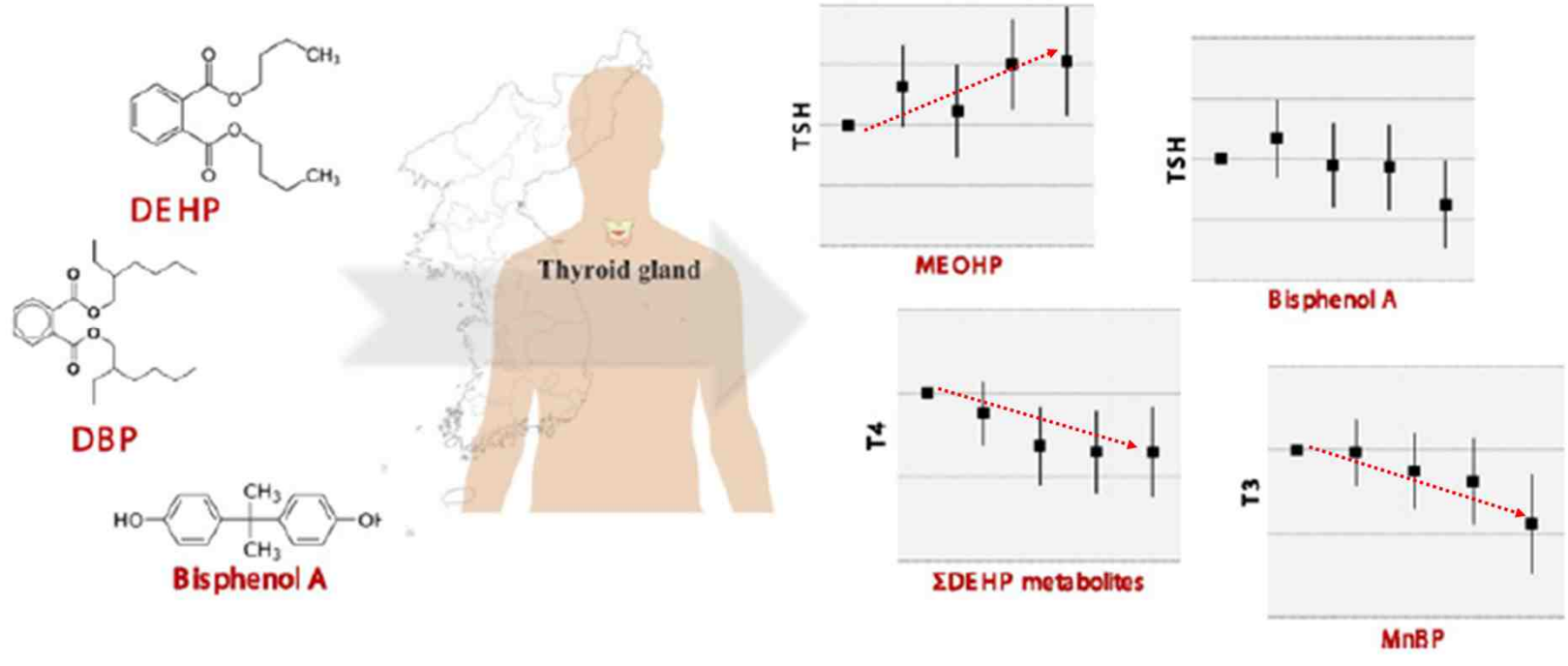


BP-3 and **DEHP** are associated with thyroid hormones

(Kim SJ et al. 2017 Environ Int)

Thyroid hormone - related

- **Phthalates and BPA in Korean general population (n=6,003)**

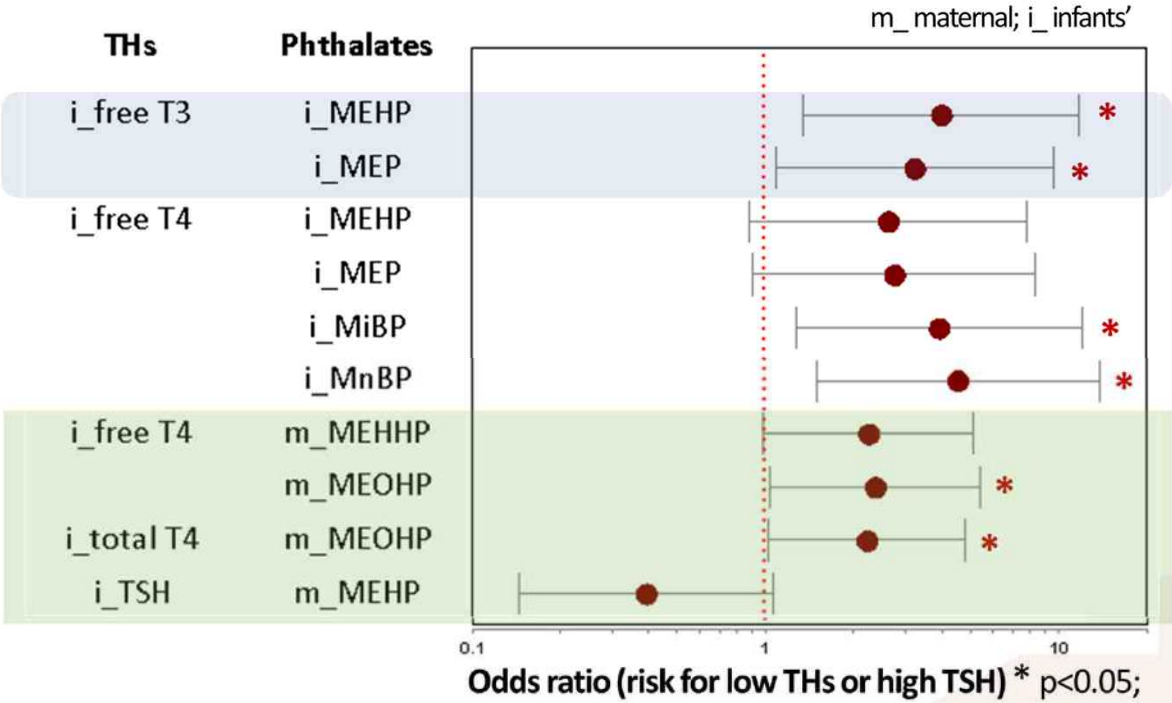


국민환경보건기초조사 결과, DEHP, DnBP, BPA가
갑상선호르몬 교란의 중요 물질

(Park CH et al. 2017 Sci Total Environ)

Thyroid hormone - related

- **Phthalates in Korean pregnant women and newborn infants (n=217)**

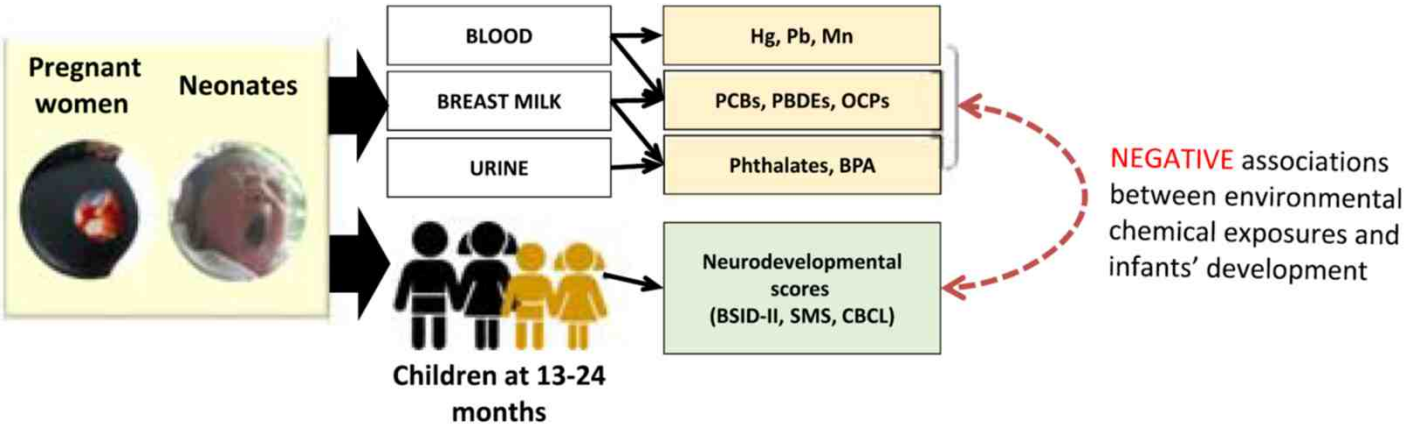


신생아소변 또는 출산시 산모 소변 중 프탈레이트가 높은 경우
갑상선호르몬(free T3, free T4, total T4)이 낮아질 위험비가 유의하게 높음

(Kim SM et al. In prep)

Neurodevelopmental impacts

- **프탈레이트/중금속/POPs 노출과 어린이 신경발달점수 (n≈150)**



Compounds	All β (95% CI)	n	Boy β (95% CI)	n	Girl β (95% CI)	n
MDI						
Urinary MEP	-2.40 (-4.39, -0.40) *	73	-1.03 (-4.55, 2.50)	36	-2.98 (-5.48, -0.48) *	37
Breastmilk MEHP	-5.60 (-11.05, -0.14) *	63	-8.26 (-16.47, -0.04) *	27	-2.04 (-9.95, 5.86)	36
PDI						
Urinary MEP	-2.25 (-4.03, -0.47) *	73	-0.25 (-3.48, 2.98)	36	-3.21 (-5.51, -0.90) *	37

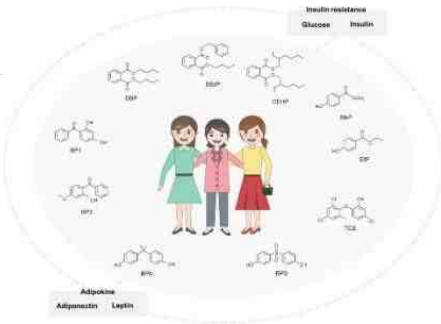
*p<0.05, adjusted for maternal age, gestational age, BMI, and maternal depression index. Use ln-transformed chemical conc.

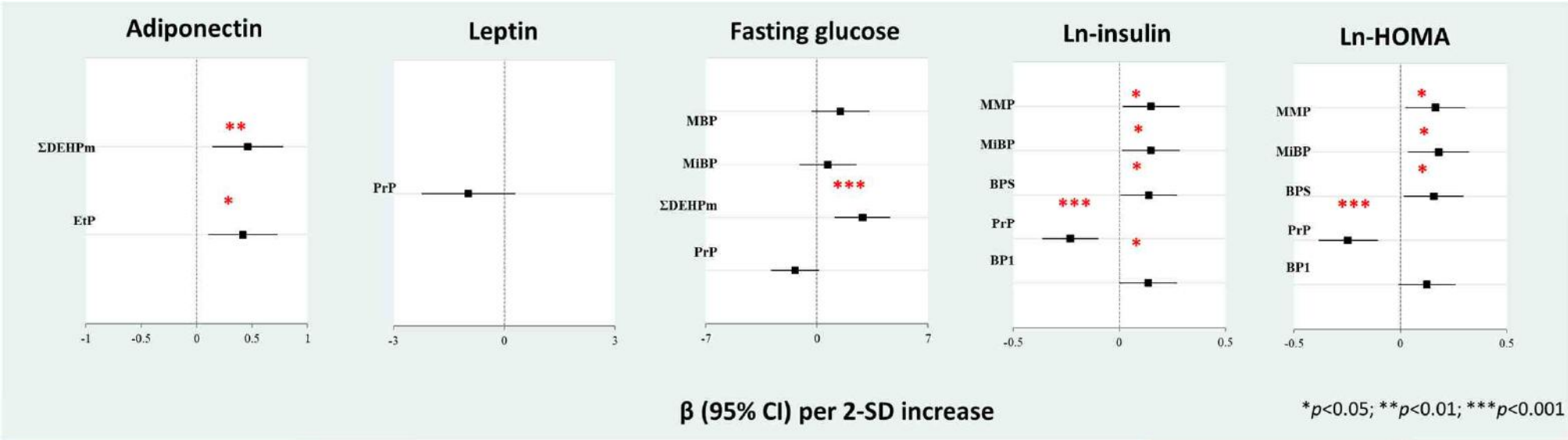
프탈레이트 노출수준이 높을수록 정신발달지수, 운동성발달지수 ↓

(Kim SM et al. Sci Total Environ 2018)

Obesity-related

- **Non-persistent EDCs in Korean adult women (n=459)**





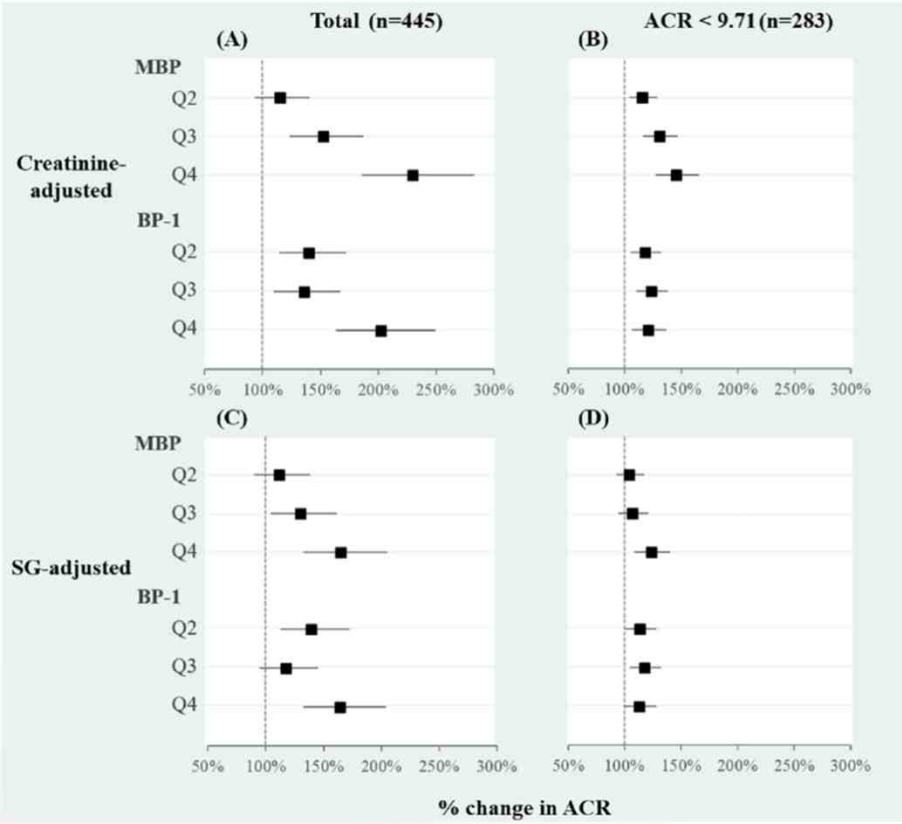
Results of multi-pollutant model with elastic net regression

프탈레이트, 에틸파라벤, BPS 노출과 당뇨병 지표와 양의 상관성

(Lee IA et al. 2019 Sci Total Environ)

Chronic kidney disease

- **Phthalates, parabens, benzophenones in Korean women (n=441)**



urinary albumin-to-creatinine ratio (ACR)

프탈레이트(MBP), 벤조페논 노출과
만성신장질환 지표(ACR)와 양의 상관관계

(Kang HB et al. Environ Int 2019)

FUTURE WORKS

Challenges in EDCs researches

- **EDCs 연구, 특히 환경역학 분야에서 느끼는 어려운 점**
  - 단면연구 특성
  - EDCs의 노출 특성
  - EDCs의 건강영향 특성

우리가 알고 싶은 것

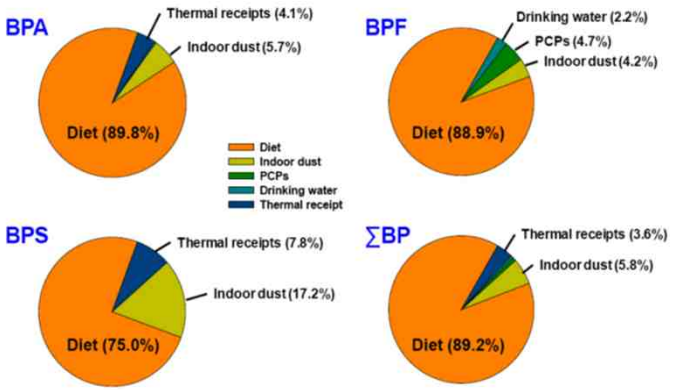
Are you being exposed?

And from WHAT?

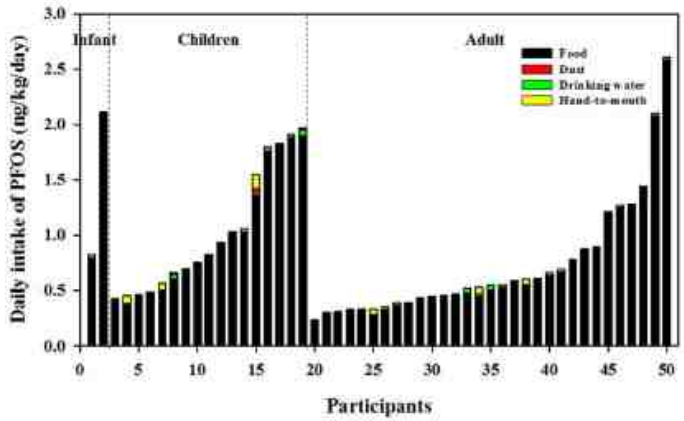
Relative source contribution
상대기여도 – 노출관리에 도움

http://BreastcancerUK.org.uk
Schecter et al., 2006 EHP

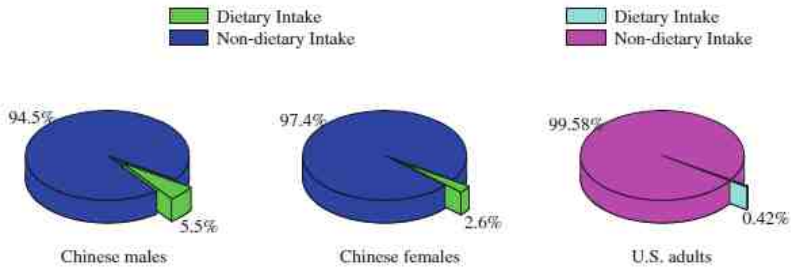
시나리오/실측 계산된 노출원별 상대기여도



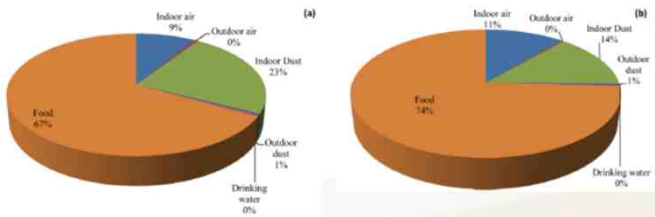
비스페놀류, 한국 성인 (Moon et al., 2017)



PFOS, 한국 50명 개인 (Kim et al., 2019)



파라벤류, 중국/미국 성인 (Ma et al., 2013)

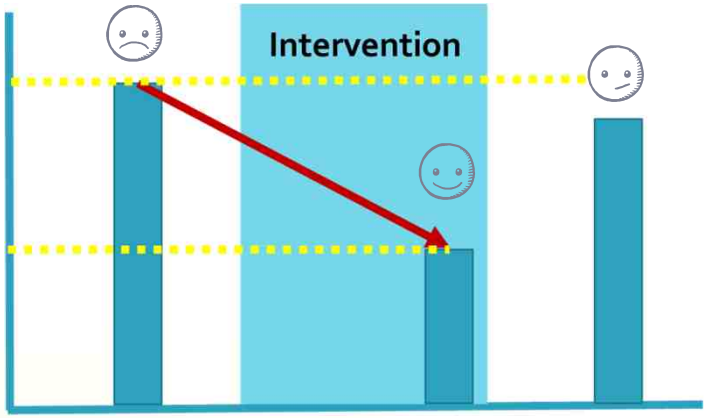


15종 프탈레이트류, 인도 성인 (Das et al., 2014)

중재연구 – 식이 프탈레이트, 비스페놀류

- **중재연구(Intervention study)**
  - 화학물질이 실제로 특정 행동(노출원 회피)을 통해 증가/감소하는지를 확인
  - 노출원의 제한을 통해 효율적이며 정량적으로 상대기여도 확인 가능

- **CASE 1: 엄마-아이 37가족 대상 코팅재, 플라스틱류를 사용하지 않는 음식 먹기 실험**
- **CASE 2: 템플스테이 참여자 15명 대상 일상식이 -> 산사음식만 5일간 먹기**



- 저감 방안(중재 내용) - 자발적 실천 권고

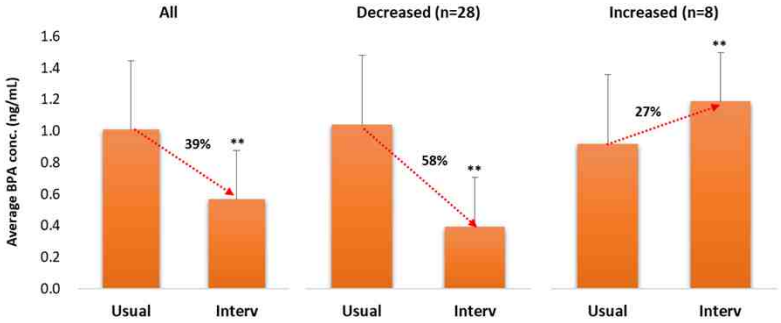
  - 캔음료, 캔식품(참치캔, 옥수수캔등) 섭취하지않기
  - 플라스틱에담긴식품섭취하지않기
  - 배달음식, 외부음식, 각종가공식품피하기
  - 밥, 채소위주의재료를먹기
  - 페트병에담긴생수마시지않기(수돗물의경우, 스테인리스용기에끓여마시기, 정수기생수가능)

중재연구 – 식이 비스페놀류

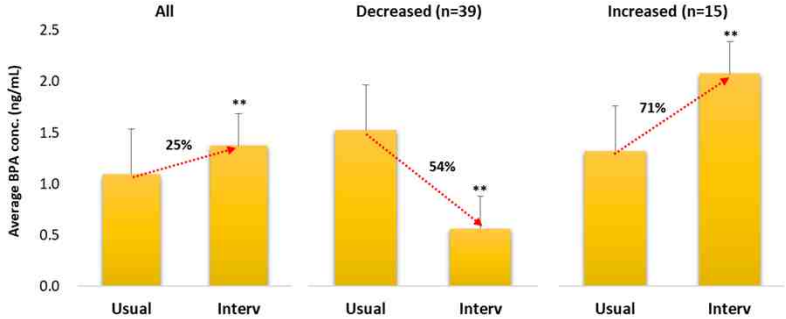
- **비스페놀 A, 비스페놀 S**

*p<0.05
**p<0.01

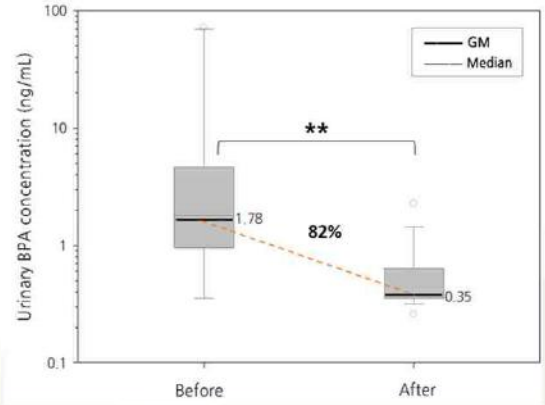
Mothers



Children

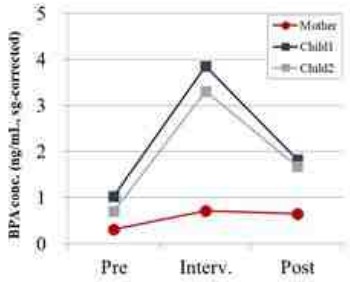


Temple-stay

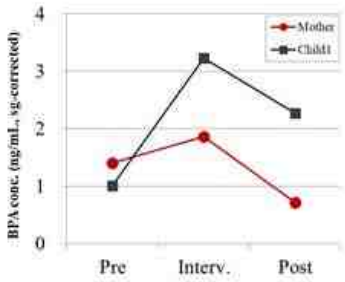


Family 1 (both increased)

ECO03



ECO15



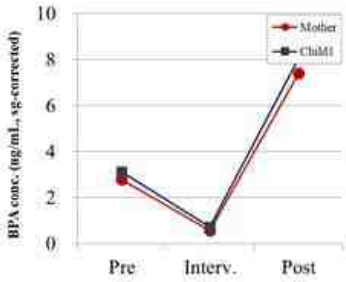
Significant exposure sources during intervention

No evidence of increased BPA only in children

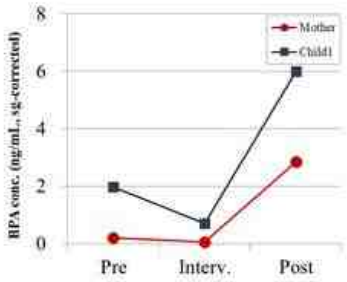
Chicken soup with rice, beef braised in soy sauce

Family 2 (both decreased)

ECO20



ECO30



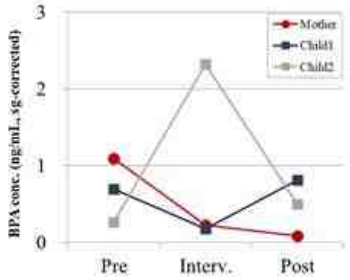
Significant restricted items in intervention period

Instant dumplings, instant rice noodle, Rolled rice with laver, Chinese-style delivery food

PET-bottled water, plastic boiling pot, plastic vial for cough-syrup intake (child)

Family 3 (decreased in mother, increased in children)

ECO02

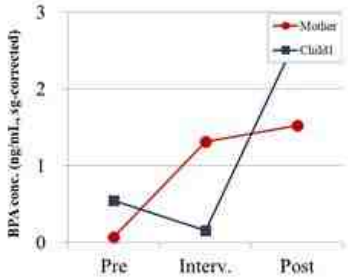


Major difference in food intake during intervention

Amond-breeze (in TetraPak) in child 2 alone

Family 4 (increased in mother, decreased in children)

ECO17



Major difference in food intake during intervention

Chinese-style spicy noodle soup, Korean formal cuisine in mother alone

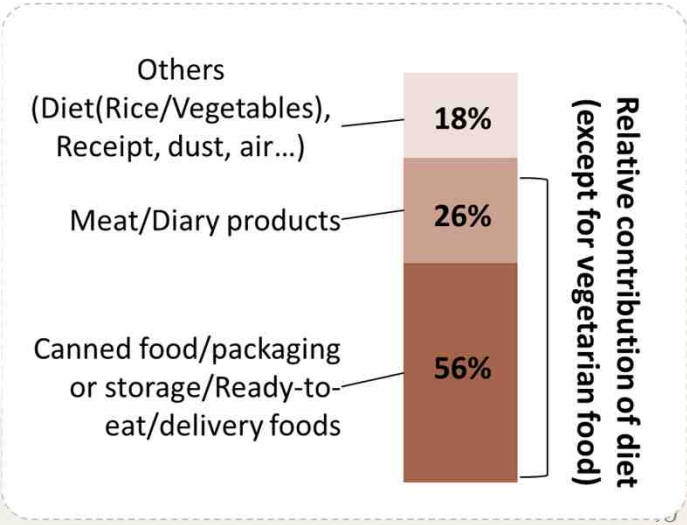
중재연구 – 식이 비스페놀류

- **비스페놀 A, 비스페놀 S**

	Percentage of people with intervention effects	Average reduction rate of BPA	Maximum reduction rate of BPA
Mothers	28 / total 36 (56%)	58 ± 29 %	93.3 %
Children	39 / total 54 (64%)	54 ± 29 %	96.0 %
Temple-stay	12 / total 15 (80%)	82 ± 13 %	99.5 %

Relative contribution of diet to total BPA body burden?

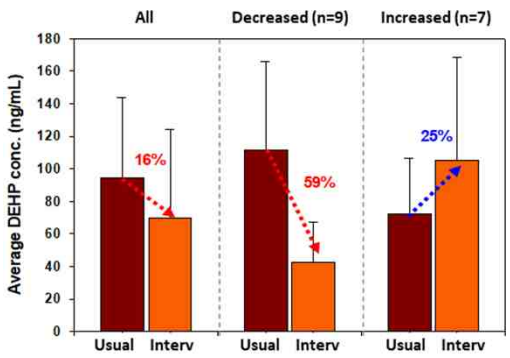
- Average 54-82%, up to 99.5%
- Relative contribution of meat/diary products to total exposure: about 26%



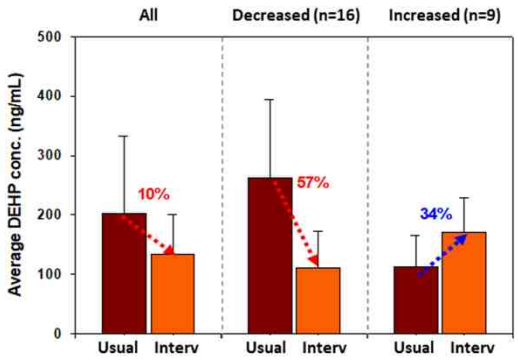
중재연구 – 식이 프탈레이트 노출

- **DEHP in both intervention studies**

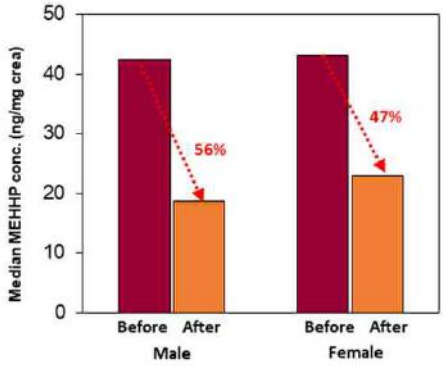
Mothers



Children



Temple-stay



	Percentage of people with intervention effects (%)	Average reduction rate of DEHP (%)	Maximum reduction rate of DEHP
Mothers	9 / total 16 (56%)	59 ± 23%	85.7 %
Children	16 / total 25 (64%)	57 ± 23%	82.6 %
Temple-stay	-	51%	-

But it's tiny portion of EDCs…

The Great Chemical Unknown

Only a tiny fraction of the compounds around us have been tested for safety

● Chemicals used by U.S. consumers and industry: 50,000 ● Tested: 300 ● Restricted: 5

Experts guesstimate that about 50,000 chemicals are used in U.S. consumer products and industrial processes. Why the uncertainty? The 1976 Toxic Substances Control Act does not require chemicals to be registered or proven safe before use. Because the Environmental Protection Agency must show, after the fact, that a substance is dangerous, it has managed to require testing of only about 300 substances that have been in circulation for decades. It has restricted applications of five.

The House Toxic Chemicals Safety Act of 2010 and the Senate Safe Chemicals Act of 2010 would require manufacturers to prove that existing and new chemicals meet specific safety criteria. Stricter scrutiny in Europe and Canada suggests that "10 to 30 percent of

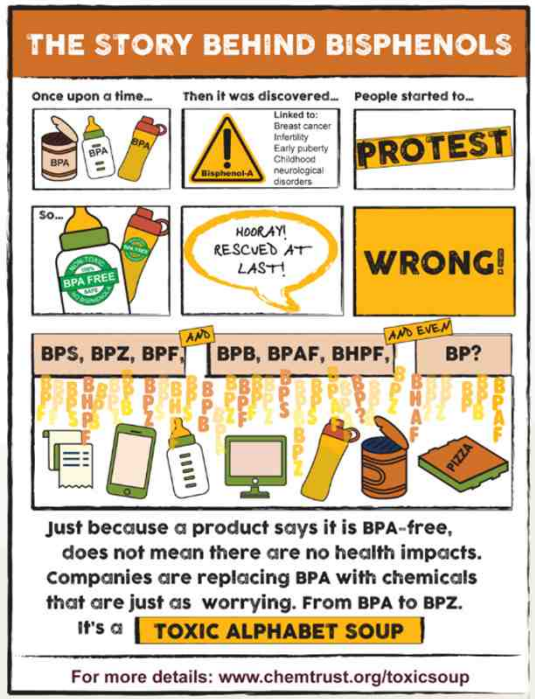
2010.11. Scientific American

EDCs: regulation still lagging behind evidence

- 개인의 노출저감 노력은 한계가 있음, 그러나 현재로서는 개인의 노력이 필요

- **규제 실효성**
  - 함량규제: 만성저농도노출에 따른 독성, 민감군 고려 어려움
  - 기존 제품, 재활용 제품은 제외
  - 어린이용품 별도 규제는 어린이를 지킬 수 있을까
    - 경고문구, 사용연령, 어린이용품 품목 설정, 실제 사용범위…

- **새로 개발된 물질**
  - '대체'물질은 모두 옛날 것보다 안전한가?
  - Positive list와 Negative list
  - 덜 해로운 대체물질을 찾기 위한 평가 체계



EDCs 노출 저감: 또 다른 어려움

- **위해성평가에서의 어려운 점**
  - 모든 시나리오에 대한 정보가 존재하지 않음
  - 오염도 자료가 부족하고 계속 바뀜
  - 독성영향 모르는 부분 많음

- **소비자 제품 중심 시나리오, 오염도 자료의 부족**
  - 일반 경피 외 구강점막, 여성외음부 노출평가를 위한 정보 부족
    - 파라벤 구강점막 흡수율은 훨씬 높음
    - 경피 PBPK 모델 개발 결과, 경구에 비해 오래 머물고 조금 배출됨
  - 제품 자체 사용량, 잔류량, 용출량 정보 부족
    - 문신용염료, 마스크팩, 섬유유연제, 주방세제 등 의류나 식기에 잔류량 정보 부족
    - 공인시험법이 없는 경우 평가 어려움
  - 오염도 수준은 계속해서 바뀜
    - 지속적 모니터링: 시기, 비용의 문제

EDCs 노출 저감: 또 다른 어려움

- **우리가 모르는 독성영향**
  - 건강영향 대비 기준치를 작성한다 해도 독성영향 모르는 부분 많음
  - EDCs의 특성
    - 용량보다 시기가 중요, 세대전이 가능성, 저용량효과
  - Key research initiatives to be supported (European parliament, 2019)
    - Epigenetics
    - Multi- and transgenerational effect
    - Microbiome effect
    - Green chemistry
    - Less studied modalities (ex. receptor-based effect)
    - Human D-R function (exposure window, low-dose effect)
  - 만성, 저농도, 혼합노출 독성영향 연구 부족

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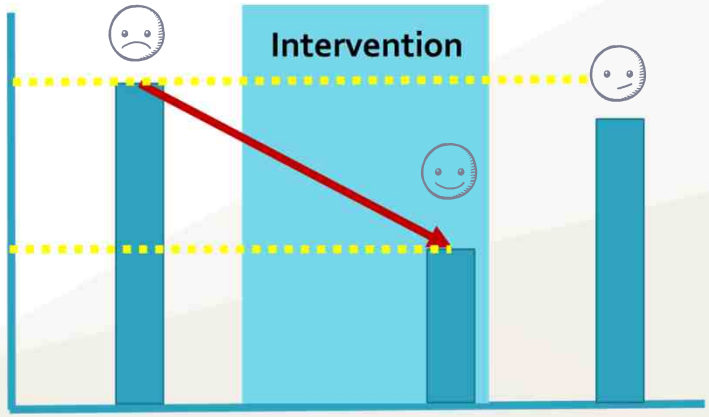
EDCs 노출 저감: 매체 중심에서 출발한 한계

- **IRAMe-ecoREA, 그 외 환경부 위해성평가 결과**
  - 많은 경우 가장 중요한 오염원은 식품

- **같은 식약처 내에서도 타 과 소관 오염원을 누락**
  - 파라벤 통합위해성평가 사례

- **수용체 중심 현재 노출수준, 건강영향의 감소가 중요**
  - 중재연구 사례
  - 일회용 생리대 건강영향 사례



THANK YOU

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