INTERFERENTI ENDOCRINI

Una grave minaccia per la salute

Effetti sul metabolismo

Udine 28 settembre 2024

Ernesto Rorai e Gustavo Mazzi

(ISDE Pordenone)

OMCeO Udine

FNOMCeO

Federazione Nazionale degli Ordini
dei Medici Chirurghi e degli Odontoiatri

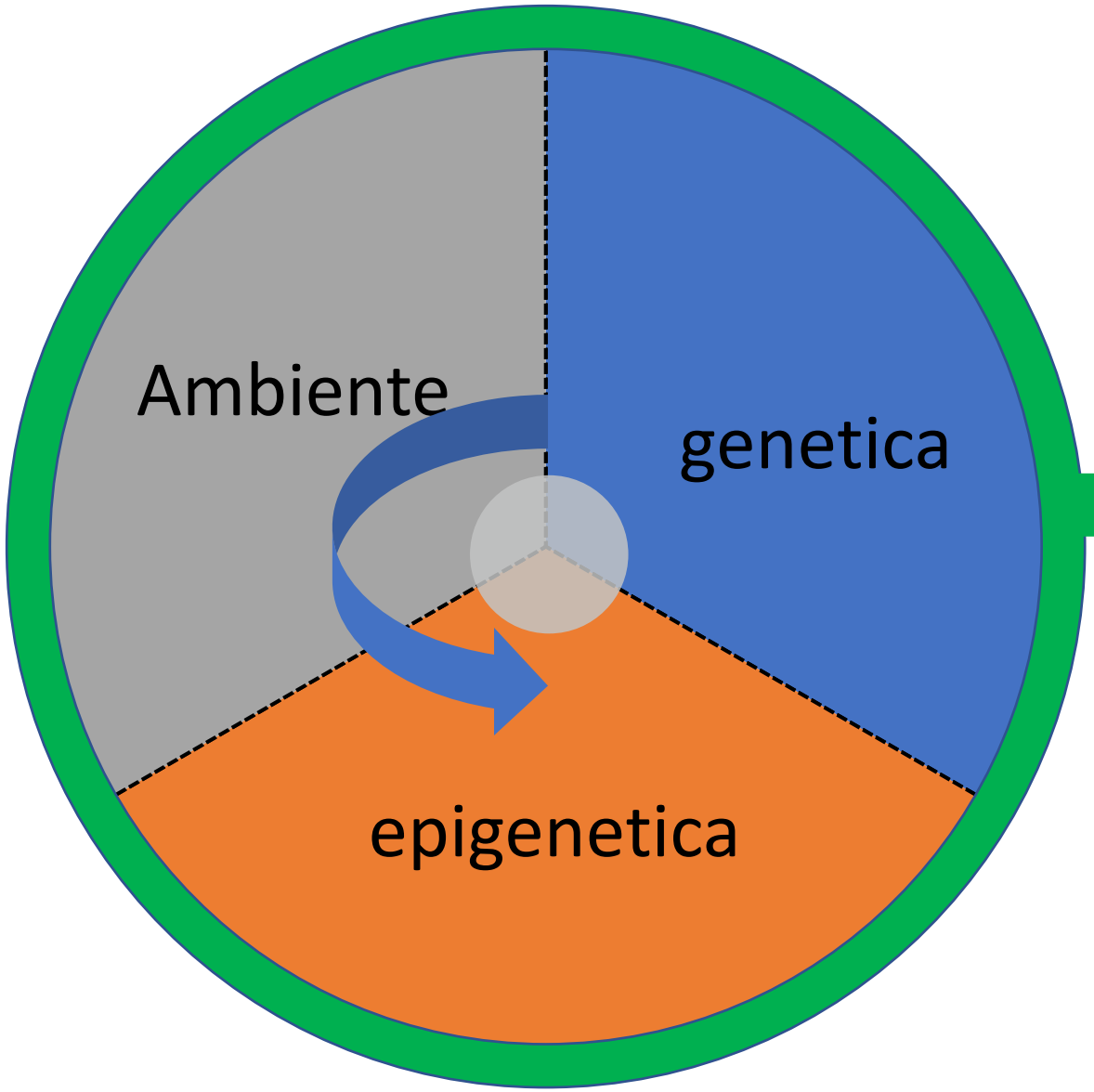
La salute della nostra popolazione sta peggiorando?

Almeno il 50% della popolazione adulta è affetta da una o più malattie croniche.

Le più frequenti sono:

- Malattie cardiovascolari
- Neoplasie
- Diabete
- Obesità
- Infertilità e disturbi del sistema riproduttivo
- Malattie della tiroide
- Sindrome depressiva e altri disturbi psichiatrici

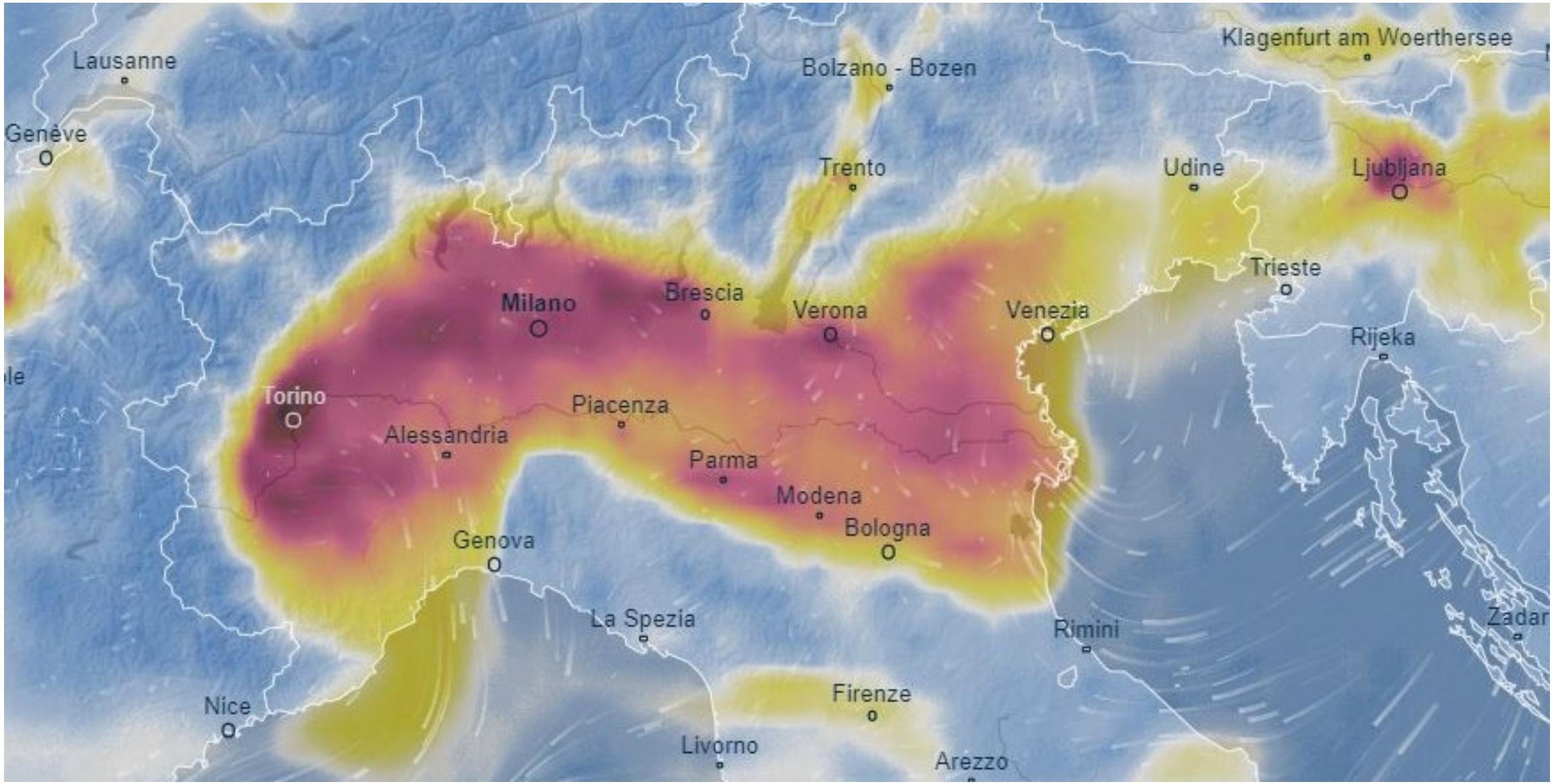
Endocrine-Disrupting Chemicals and Human Health, R. Thomas Zoeller and Jerrold J. Heindel, in DeGroot's Endocrinology: Basic Science and Clinical Practice 8th ed. 2023, pagg 2305-2322



Fenotipo:
Ciò che noi siamo
o che diventiamo

Dottore, perché mi sono ammalato?

Effetti metabolici dell’inquinamento dell’aria

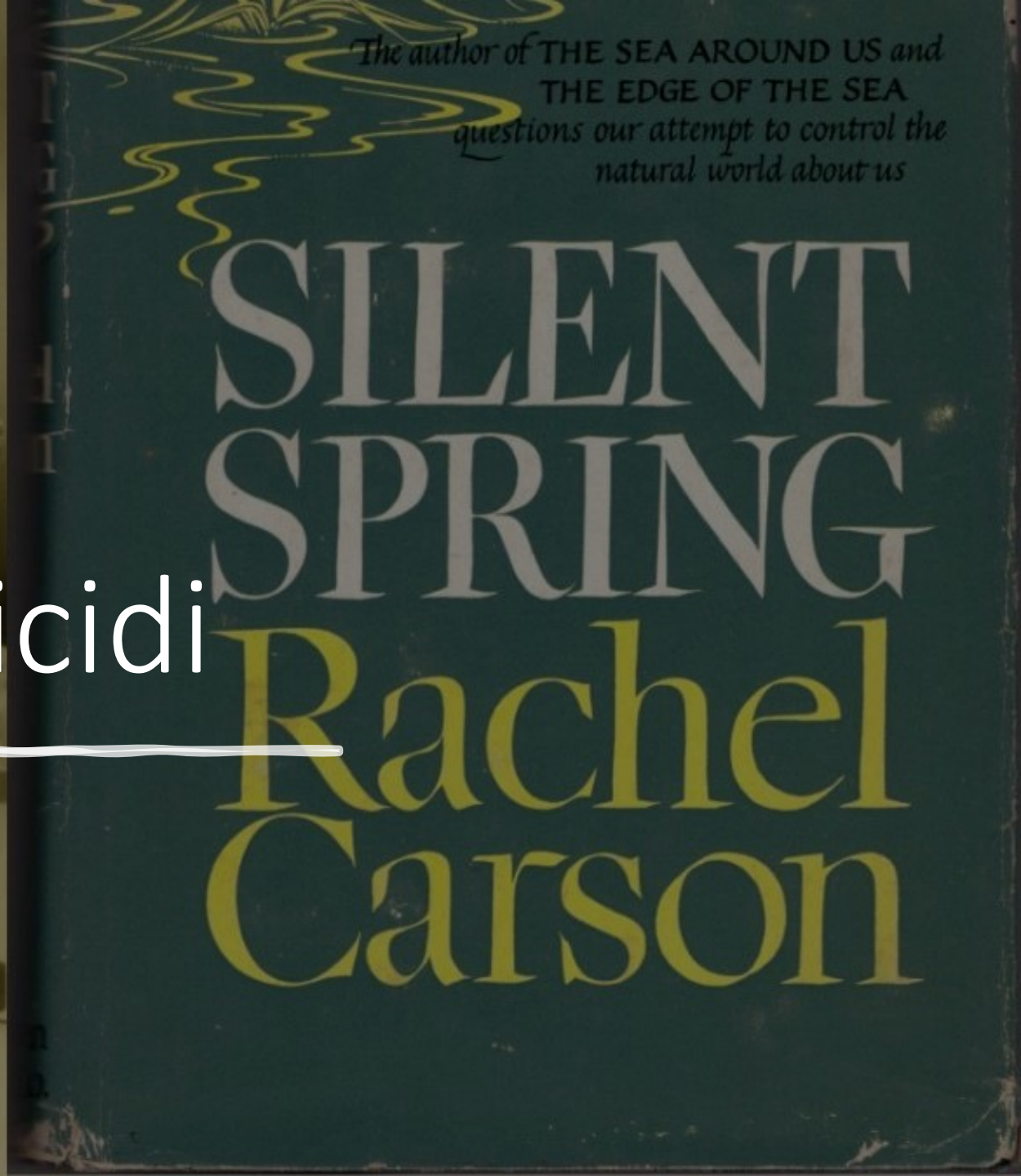

Lausanne
Genève
Bolzano - Bozen
Klagenfurt am Woerthersee
Trento
Udine
Ljubljana
Trieste
Milano
Brescia
Verona
Venezia
Rijeka
Torino
Piacenza
Alessandria
Parma
Modena
Bologna
Genova
La Spezia
Rimini
Zadar
Nice
Firenze
Livorno
Arezzo

PM10 – PM 2,5

Plastica, alimenti, stile di vita

Tim Noble
Sue Webster

Pesticidi


The author of THE SEA AROUND US and
THE EDGE OF THE SEA
questions our attempt to control the
natural world about us
SILENT
SPRING
Rachel
Carson

Rachel Carson 1907 - 1964

- Biologa, laureata nel1932 (John Hopkins University), non ha i mezzi per conseguire un dottorato. Insegna alla scuola estiva dell'università, fa ricerca al dipartimento di zoologia dell'università del Maryland, diventerà una brillante giornalista e ricercatrice di valore.
- 1955 la comunità scientifica è allarmata per le morie ricorrenti di pesci nel Mississippi; è l'epoca delle nuvole di DDT e altri pesticidi sparse con gli aerei, per conto del ministero dell'agricoltura o di aziende agro-alimentari. La libertà d'inquinare è garantita dall'assenza di leggi a difesa dell'ambiente e dei suoi abitanti, e gli effetti sulla flora e la fauna sono evidenti. Rachel Carson si carica l'onere di farsene portavoce. Una minoranza ritiene che i benefici per l'agricoltura prevalgano su una tossicità "ancora da dimostrare" e sulla quale "non c'è consenso" (frasi di attualità anche a proposito dei cambiamenti climatici).
- Nell'estate 1962 il «New Yorker» pubblica le prime puntate di *Primavera silenziosa.* I produttori di pesticidi incaricano un loro comitato di scienziati di denunciare l'inaffidabilità dell'autrice. Parte una campagna denigratoria contro quella «zitella» frustrata, isterica e forse comunista, che vuol privare i figli altrui dei vantaggi del progresso. Nonostante sia indebolita dalla chemioterapia per il cancro alla mammella, lei testimonia davanti alla commissione del Congresso, e al comitato di esperti convocati dal presidente Kennedy per accertare la validità delle sue affermazioni. Il rapporto degli esperti esce nel maggio 1963 e le dà ragione.
- Muore l'anno successivo a Rockville nel Maryland.

2012 – Theo Colborn
Lettera al Presidente
«…abbiamo finora pensato che il principale rischio dell'inquinamento fosse il contributo all'insorgenza di tumori. Gran parte della ricerca è stata indirizzata al rapporto tra sostanze tossiche e cancro.
Ebbene, altri effetti delle sostanze tossiche sono ben più frequenti; mi riferisco ai disturbi neurologici infantili, come deficit di attenzione/iperattività, autismo e sindromi correlate, all'obesità, al diabete, ai disturbi della differenziazione sessuale e della fertilità...
Questi fenomeni sono dovuti all'interferenza di comuni inquinanti con il sistema endocrino…»

THEO COLBORN (1927-2014)

- Farmacista e poi agricoltore,
- Nel 1985, a 58 anni di età, dopo il raggiungimento della maggiore età dei suoi 4 figli, ottiene il dottorato di ricerca in zoologia con tesi su epidemiologia, tossicologia e chimica dell'acqua.
- Dopo anni di studio e di tessitura di una rete interdisciplinare, riesce ***a mettere insieme 16 discipline scientifiche differenti,*** tra cui Endocrinologia, Tossicologia, Ecologia, Farmacologia e Antropologia e nel 1991 in un congresso a Racine nel Wisconsin raccoglie i dati sugli effetti endocrini delle sostanze inquinanti.
- In tale occasione nasce il termine di «interferente endocrino» (Endocrine Disrupting Chemical)

Endocrine Disrupting Chemicals (EDC) [Interferenti endocrini]

Wingspread Conference Center

Racine, Wisconsin

Luglio 1991

Theo Colborn

(Theodora Emily Colborn

U.S. Environmental Protection Agency)

- **Un grande numero di sostanze chimiche alterano i sistemi endocrini:**
  - Alcuni pesticidi
  - Alcuni prodotti di sintesi
  - Alcuni metalli pesanti
- **Effetti già osservati negli animali selvatici:**
  - Disfunzione tiroidea
  - Ridotta fertilità
  - Insuccesso nella schiusa delle uova
  - Anomalie metaboliche
  - Demascolinizzazione
  - Compromissione del sistema immunitario

Executive Summary to EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals

A. C. Gore, V. A. Chappell, S. E. Fenton, J. A. Flaws, A. Nadal, G. S. Prins, J. Toppari, and R. T. Zoeller

Pharmacology and Toxicology (A.C.G.), College of Pharmacy, The University of Texas at Austin, Austin, Texas 78734; Division of the National Toxicology Program (V.A.C., S.E.F.), National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, North Carolina 27709; Department of Comparative Biosciences (J.A.F.), University of Illinois at Urbana-Champaign, Urbana, Illinois 61802; Institute of Bioengineering and CIBERDEM (A.N.), Miguel Hernandez University of Elche, 03202 Elche, Alicante, Spain; Departments of Urology, Pathology and Physiology & Biophysics (G.S.P.), College of Medicine, University of Illinois at Chicago, Chicago, Illinois, 60612; Departments of Physiology and Pediatrics (J.T.), University of Turku and Turku University Hospital, 20520 Turku, Finland; and Biology Department (R.T.Z.), University of Massachusetts at Amherst, Amherst, Massachusetts 01003

This Executive Summary to the Endocrine Society's second Scientific Statement on environmental endocrine-disrupting chemicals (EDCs) provides a synthesis of the key points of the complete statement. The full Scientific Statement represents a comprehensive review of the literature on seven topics for which there is strong mechanistic, experimental, animal, and epidemiological evidence for endocrine disruption, namely: obesity and diabetes, female reproduction, male reproduction, hormone-sensitive cancers in females, prostate cancer, thyroid, and neurodevelopment and neuroendocrine systems. EDCs such as bisphenol A, phthalates, pesticides, persistent organic pollutants such as polychlorinated biphenyls, polybrominated diethyl ethers, and dioxins were emphasized because these chemicals had the greatest depth and breadth of available information. The Statement also included thorough coverage of studies of developmental exposures to EDCs, especially in the fetus and infant, because these are critical life stages during which perturbations of hormones can increase the probability of a disease or dysfunction later in life. A conclusion of the Statement is that publications over the past 5 years have led to a much fuller understanding of the endocrine principles by which EDCs act, including nonmonotonic dose-responses, low-dose effects, and developmental vulnerability. These findings will prove useful to researchers, physicians, and other healthcare providers in translating the science of endocrine disruption to improved public health. (*Endocrine Reviews* 36: 593–602, 2015)

National Library of Medicine
National Center for Biotechnology Information

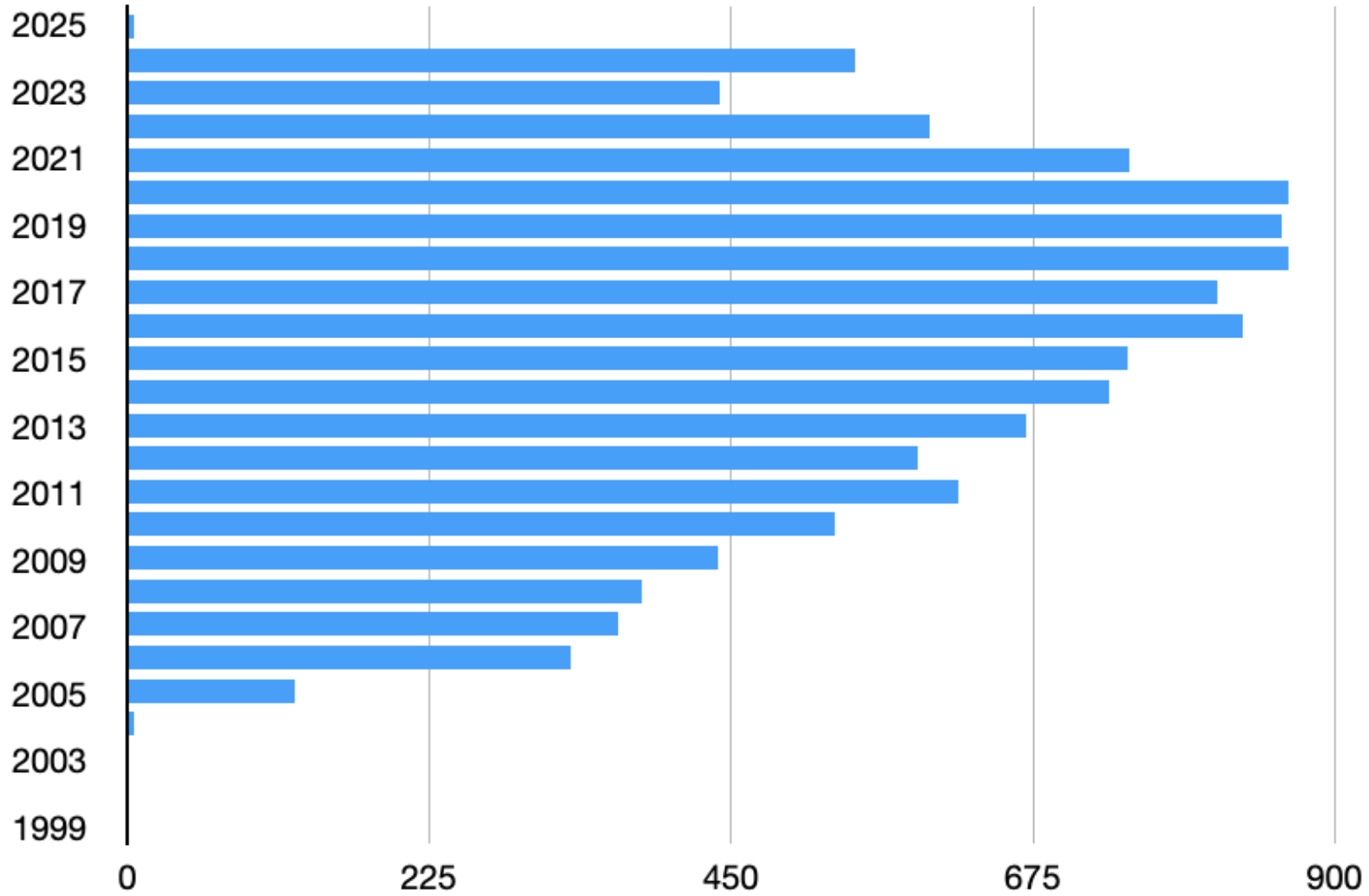
Log in

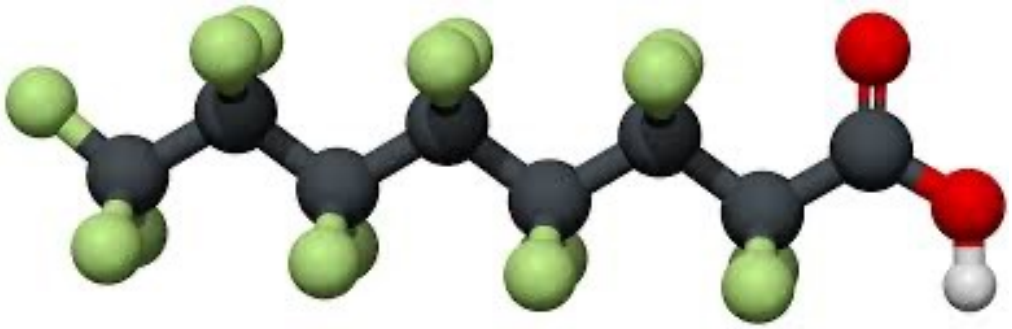
PubMed®

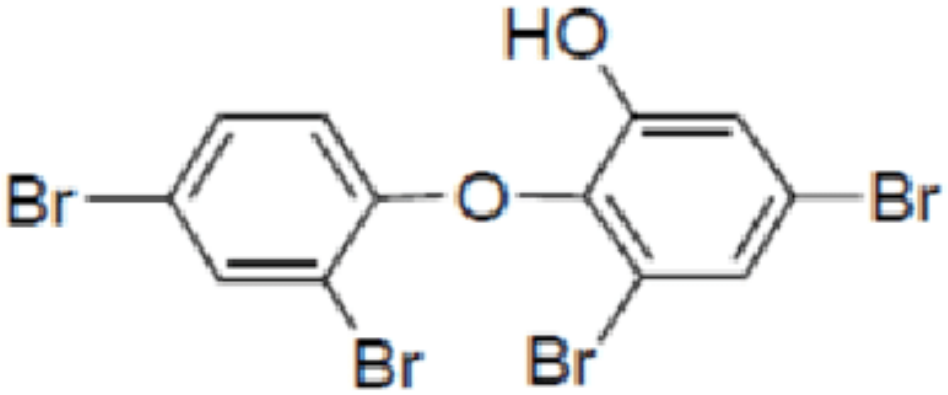
"Endocrine Disruptors"[Mesh]

Search

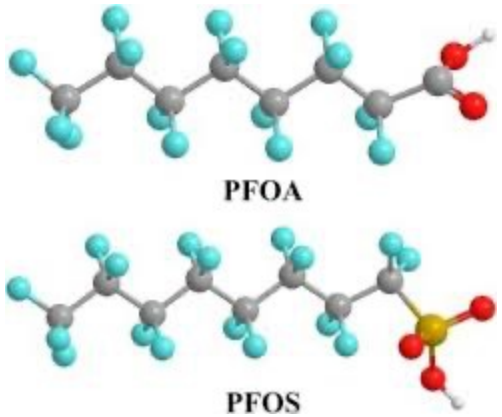
Advanced Create alert Create RSS User Guide

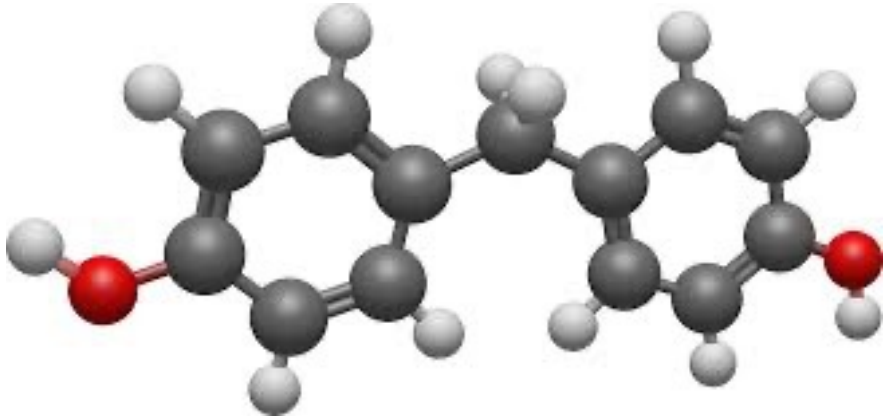




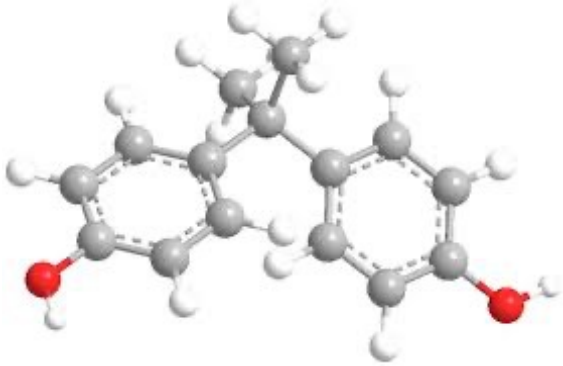


PBDE



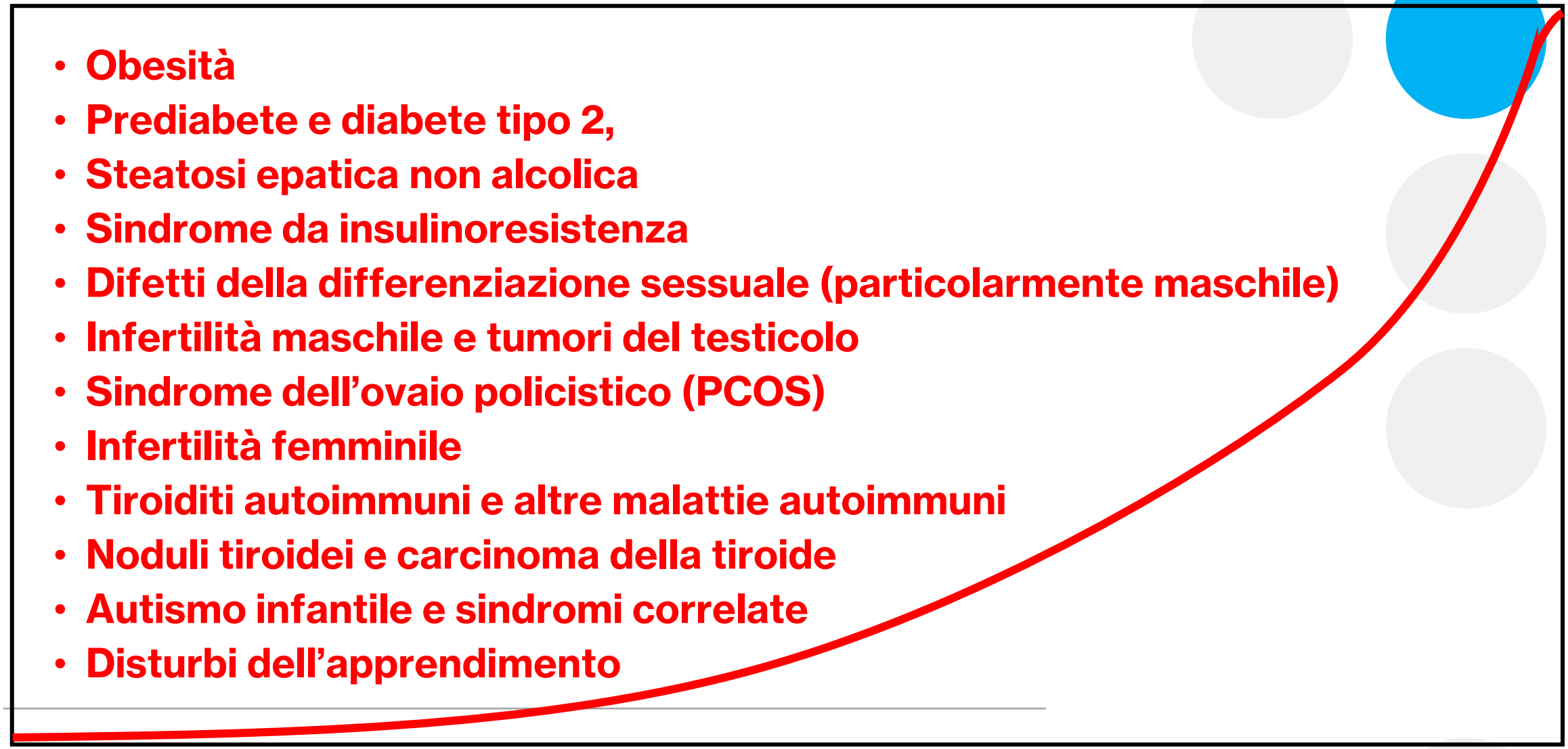


BPA



Malattie in rapido aumento ed interferenti endocrini

- Obesità
- Prediabete e diabete tipo 2,
- Steatosi epatica non alcolica
- Sindrome da insulinoresistenza
- Difetti della differenziazione sessuale (particolarmente maschile)
- Infertilità maschile e tumori del testicolo
- Sindrome dell'ovaio policistico (PCOS)
- Infertilità femminile
- Tiroiditi autoimmuni e altre malattie autoimmuni
- Noduli tiroidei e carcinoma della tiroide
- Autismo infantile e sindromi correlate
- Disturbi dell'apprendimento



Patologia dell'informazione

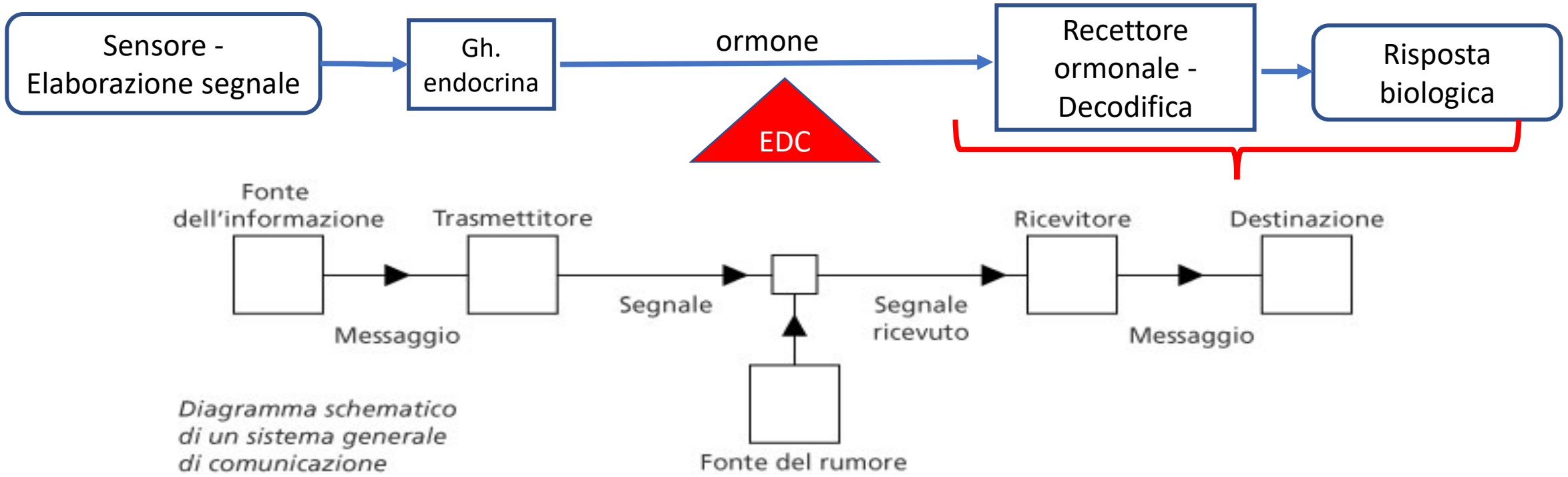
- Tossicità «tradizionale»:
  - legame covalente con strutture chimiche cellulari bersaglio della tossicità
  - Produzione di sostanze metabolicamente attive
  - Effetti ossidativi o composti reattivi
  - Mutagenicità e carcinogenicità
- Interferenza endocrina: capacità di alterare il normale flusso di informazioni tra cellula e cellula mediata dal sistema endocrino.
  - Almeno dieci i meccanismi identificati finora, dalla diretta interazione con i recettori ormonali alle alterazioni epigenetiche qualitative e quantitative della produzione di ormoni o dei relativi sistemi recettoriali.

Modelli matematici

Available online at www.sciencedirect.com
ScienceDirect
Current Opinion in Endocrine and Metabolic Research
ELSEVIER
Reviews

Decoding cellular communication: An information theoretic perspective on cytokine and endocrine signaling

Fred Schaper[1,2,3], Tomasz Jetka[4] and Anna Dittrich[1,2,3]



Current Opinion in Endocrine and Metabolic Research 2022, 24:100351

Giovanni Federspil 1980


Il diavolo nei dettagli

Crollo di un dogma

- Paracelso 1500:
- E’ la dose che fa il veleno

- *EDC - 2022: è l’informazione contenuta nella molecola che fa il veleno*

ISSN 2472-1972

Thresholds and Endocrine Disruptors: An Endocrine Society Policy Perspective

Barbara Demeneix,[1] Laura N. Vandenberg,[2] Richard Ivell,[3] and R. Thomas Zoeller,[4,5]

[1]UMR 7221, Muséum National d´Histoire Naturelle, Département Régulation Développement et Diversité Moléculaire, Paris, France 75231; [2]Department of Environmental Health Sciences, School of Public Health and Health Sciences, University of Massachusetts–Amherst, Amherst, Massachusetts 01003; [3]School of Biosciences, University of Nottingham, Sutton Bonington, UK; [4]Morrill Science Center, Department of Biology, University of Massachusetts–Amherst, Amherst Massachusetts 01003; and [5]School of Science and Technology, Örebro University, SE-701 82, Örebro Sweden

ORCiD number: 0000-0001-6513-2109 (R. Ivell); 0000-0002-7485-2658 (R. T. Zoeller).

The concept of a threshold of adversity in toxicology […] In the context of endocrine-disrupting chemicals (EDCs),… is demonstrably inappropriate. First, the efficacy of a hormone on different endpoints can vary by several orders of magnitude. This feature of hormone action also applies to EDCs that can interfere with that hormone. […] Second, the biological events controlled by hormones in development not only change as development proceeds but are different from events controlled by hormones in the adult. […]

n engl j med 381;25 nejm.org December 19, 2019

The NEW ENGLAND JOURNAL of MEDICINE

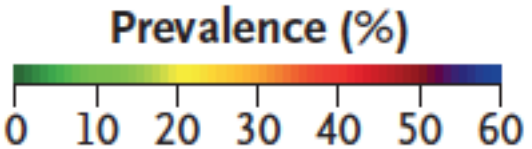
SPECIAL ARTICLE

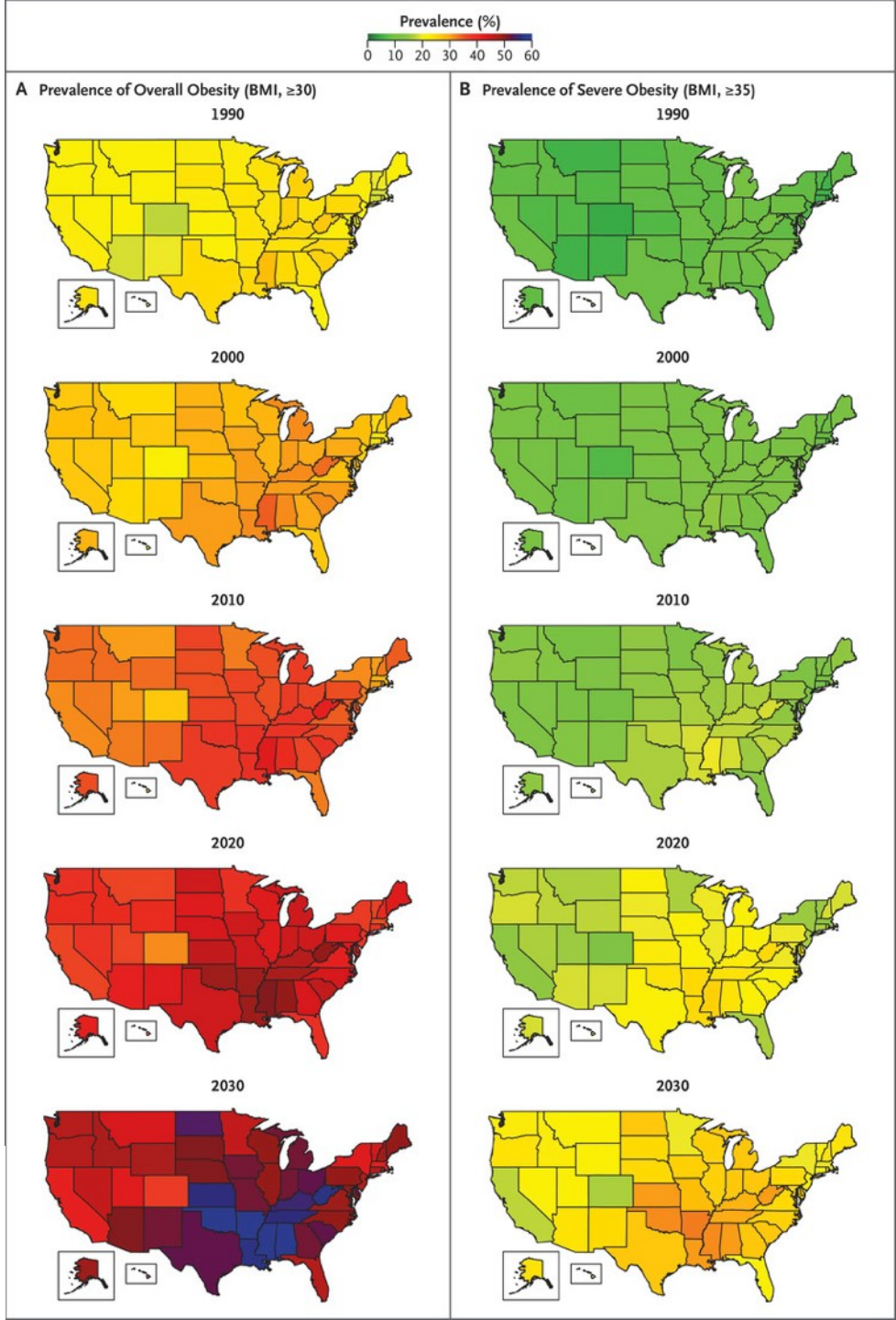
Projected U.S. State-Level Prevalence of Adult Obesity and Severe Obesity

Zachary J. Ward, M.P.H., Sara N. Bleich, Ph.D., Angie L. Cradock, Sc.D., Jessica L. Barrett, M.P.H., Catherine M. Giles, M.P.H., Chasmine Flax, M.P.H., Michael W. Long, Sc.D., and Steven L. Gortmaker, Ph.D.

ABSTRACT

y epidemic has been well documented, less is known
level. Current estimates are based on body measures
ves that underestimate the prevalence of obesity, es-





The NEW ENGLAND JOURNAL of MEDICINE

January 23, 1986
N Engl J Med 1986; 314:193-198
DOI: 10.1056/NEJM198601233140401

ORIGINAL ARTICLE ARCHIVE

An Adoption Study of Human Obesity

Albert J. Stunkard, M.D., Thorkild I.A. Sørensen, Dr.med., Craig Hanis, Ph.D., Thomas W. Teasdale, M.A., Ranajit Chakraborty, Ph.D., William J. Schull, Ph.D., and Fini Schulsinger, DR.MED.

Abbiamo esaminato il contributo dei fattori genetici e dell'ambiente familiare di 540 danesi adulti adottati [in età infantile]…c'era una forte relazione statistica tra il peso degli adottati e quello dei genitori biologici [particolarmente della madre]; nessuna relazione invece con il peso dei genitori adottivi.
…ne abbiamo concluso che i fattori genetici hanno un ruolo importante nel determinare l'obesità in età adulta, mentre l'ambiente familiare da solo non ha apparentemente alcun effetto.

Il paradosso dei figli adottivi

International Journal of Obesity (2010) 34, 29–40

0307-0565/10 $32.00
www.nature.com/ijo

PEDIATRIC REVIEW

The genetic and environmental influences on childhood obesity: a systematic review of twin and adoption studies

K Silventoinen[1,2], B Rokholm[3], J Kaprio,[2,4,5] and TIA Sørensen[3]

[1]Department of Sociology, Population Research Unit, University of Helsinki, Helsinki, Finland; [2]Department of Public Health, University of Helsinki, Helsinki, Finland; [3]Institute of Preventive Medicine, Copenhagen University Hospital, Centre for Health and Society, Copenhagen, Denmark; [4]Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, Finland and [5]Institute for Molecular Medicine FIMM, Helsinki, Finland

In this systematic review, we aimed to collect together all previous twin and adoption studies on childhood and adolescent obesity up to the age of 18 years. Using several sources, we identified nine twin and five adoption studies; all of these studies had used relative weight as an indicator of obesity. Except the two twin studies from the Korean population, all studies represented Caucasian populations. In a meta-analysis of these twin studies, we found that genetic factors had a strong effect on the variation of body mass index (BMI) at all ages. The common environmental factors showed a substantial effect in mid-childhood, but this effect disappeared at adolescence. Adoption studies supported the role of family environment in childhood obesity as correlations were found between adoptees and adoptive parents; however, correlations were substantially stronger between parents and their biological offspring, further supporting the importance of genetic factors. In the future, more studies implementing genetic and environmental measures into twin models are needed as they allow estimation of the proportion of total genetic variation explained by candidate genes and analyses of gene–environment interactions. More studies of genetic architecture in non-Caucasian populations, of gene–environment interactions, and of body composition and body fat distribution are needed.

International Journal of Obesity (2010) **34**, 29–40; doi:10.1038/ijo.2009.177; published online 15 September 2009

however, correlations were substantially stronger between parents and their biological offspring,

Genetic and environmental effects on body mass index from infancy to the onset of adulthood: an individual-based pooled analysis of 45 twin cohorts participating in the COllaborative project of Development of Anthropometrical measures in Twins (CODATwins) study[1–3]

Data were available for 87,782 complete twin pairs from 0.5 to 19.5 y…

The proportion of BMI variation explained by additive genetic factors was lowest at 4 y of age in boys (a2 =0.42) and girls (a2 = 0.41) and then generally increased to 0.75 inboth sexes at 19 y of age. This was because of a stronger influence of environmental factors shared by co-twins in midchildhood. After 15 y of age, the effect of shared environment was not observed.

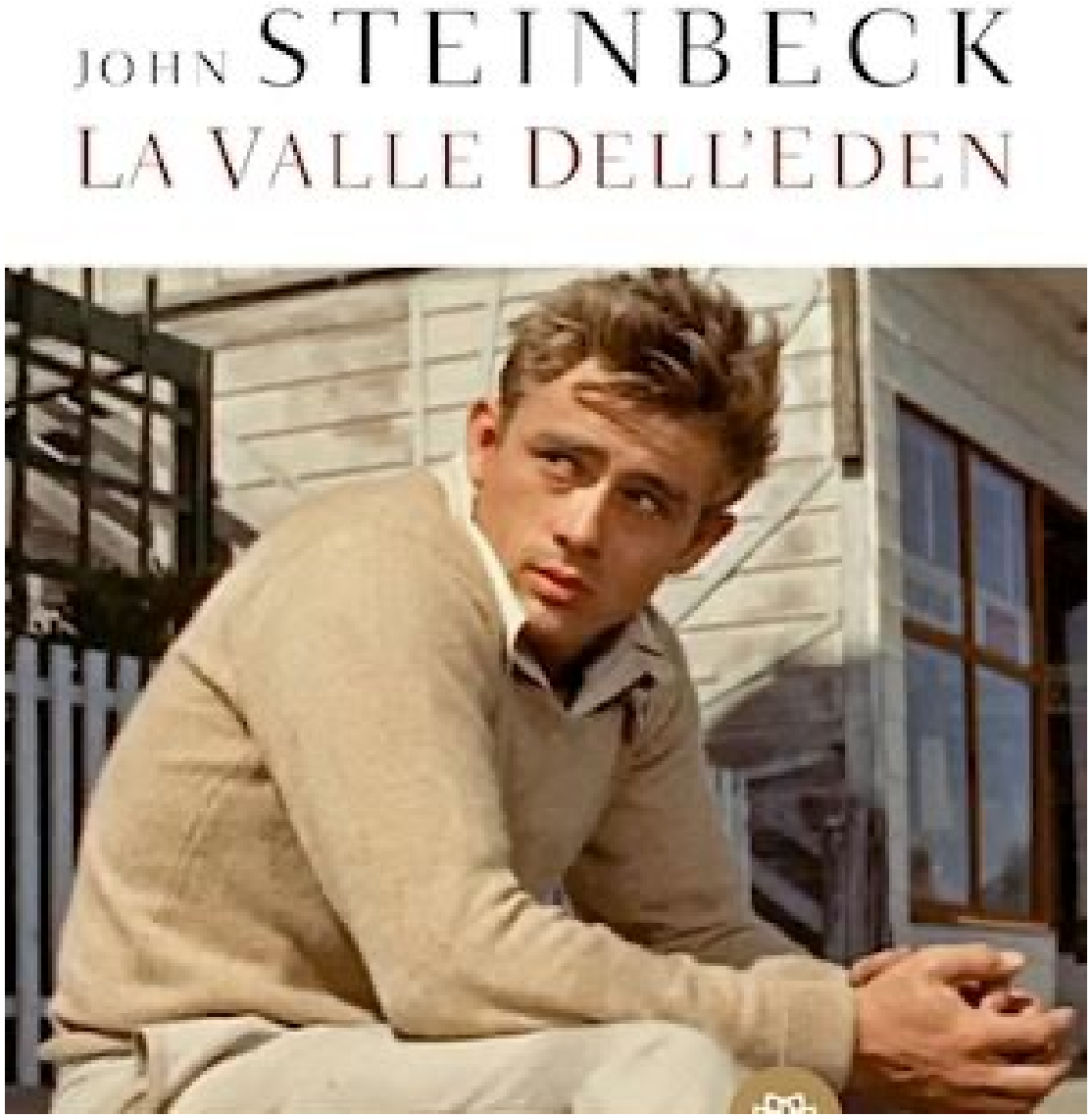
Studio su 87’782 coppie di gemelli: i fattori ambientali possono modificare l’andamento del peso durante l’infanzia, successivamente il loro ruolo progressivamente si riduce; dopo i 15 anni l’effetto dell’ambiente non è più rilevabile [e i fattori genetici rimangono dominanti].

Am J Clin Nutr 2016;104:371–9.


Monterey Bay
Salinas
Monterey
Chualar Cr.
San Benito
SAN BENITO COUNTY
California
Aqueduct
Carmel
Chalone Cr.
Soledad
MONTEREY COUNTY
Greenfield
FRESNO COUNTY
Arroyo Seco
Reliz Cr.
Lewis Cr.
San Lorenzo Cr.
King City
Coalinga
Pacific Ocean
Salinas
San Ardo
Pancho Rico Cr.
San Antonio
Nacimiento
Lake San Antonio
Big Sandy Cr.
Cholame Cr.
KINGS COUNTY
Lake Nacimiento
Estrella
Branch
Paso Robles
Huerhuero Cr.
Coastal
San Juan Cr.
Cambria
Atascadero
Morro Bay
Santa Margarita Lake
San Luis Obispo
SAN LUIS OBISPO COUNTY
Pismo Beach
NEV.
San Francisco
CALIF.
Los Angeles
0 10 20 30 40 miles

CHAMACOS Study:

Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS)



Prenatal and Postnatal Bisphenol A Exposure and Body Mass Index in Childhood in the CHAMACOS Cohort

Kim G. Harley,[1] Raul Aguilar Schall,[1] Jonathan Chevrier,[1] Kristin Tyler,[1] Helen Aguirre,[1] Asa Bradman,[1] Nina T. Holland,[1] Robert H. Lustig,[2] Antonia M. Calafat,[3] and Brenda Eskenazi[1]

[1]Center for Environmental Research and Children's Health, School of Public Health, University of California, Berkeley, Berkeley, California, USA; [2]Division of Endocrinology, University of California, San Francisco, San Francisco, California, USA; [3]Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

American Journal of Epidemiology

Vol. 179, No. 11
DOI: 10.1093/aje/kwu046
Advance Access publication:
April 9, 2014

Original Contribution

Prenatal Exposure to Dichlorodiphenyltrichloroethane and Obesity at 9 Years of Age in the CHAMACOS Study Cohort

Marcella Warner*, Amelia Wesselink, Kim G. Harley, Asa Bradman, Katherine Kogut, and Brenda Eskenazi

* Correspondence to Dr. Marcella Warner, Center for Environmental Research and Children's Health, School of Public Health, University of California, 1995 University Avenue, Suite 265, Berkeley, CA 94720-7392 (e-mail: mwarner@berkeley.edu).

Published in final edited form as:
Pediatr Res. 2017 September ; 82(3): 405–415. doi:10.1038/pr.2017.112.

Association of prenatal urinary phthalate metabolite concentrations and childhood BMI and obesity

Kim G. Harley[1], **Kimberly Berger**[1], **Stephen Rauch**[1], **Katherine Kogut**[1], **Birgit Claus Henn**[2], **Antonia M. Calafat**[3], **Karen Huen**[1], **Brenda Eskenazi**[1], and **Nina Holland**[1]

[1]Center for Environmental Research and Children's Health (CERCH), School of Public Health, University of California, Berkeley, CA

[2]Department of Environmental Health, Boston University School of Public Health, Boston, Massachusetts

[3]Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia

We measured urinary concentrations of 11 phthalate metabolites collected twice during pregnancy from mothers participating in the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) cohort study (N = 345). Height, weight, waist circumference, and percent body fat were assessed in their children between 5 and 12 years of age.[…] Metabolites of diethyl phthalate (DEP), di-n -butyl phthalate (DBP), butyl benzyl phthalate, and di(2-ethylhexyl) phthalate (DEHP) were positively associated with BMI z -score, waist circumference z -score, and percent body fat at multiple ages.

A Section 508–conformant HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1408417.

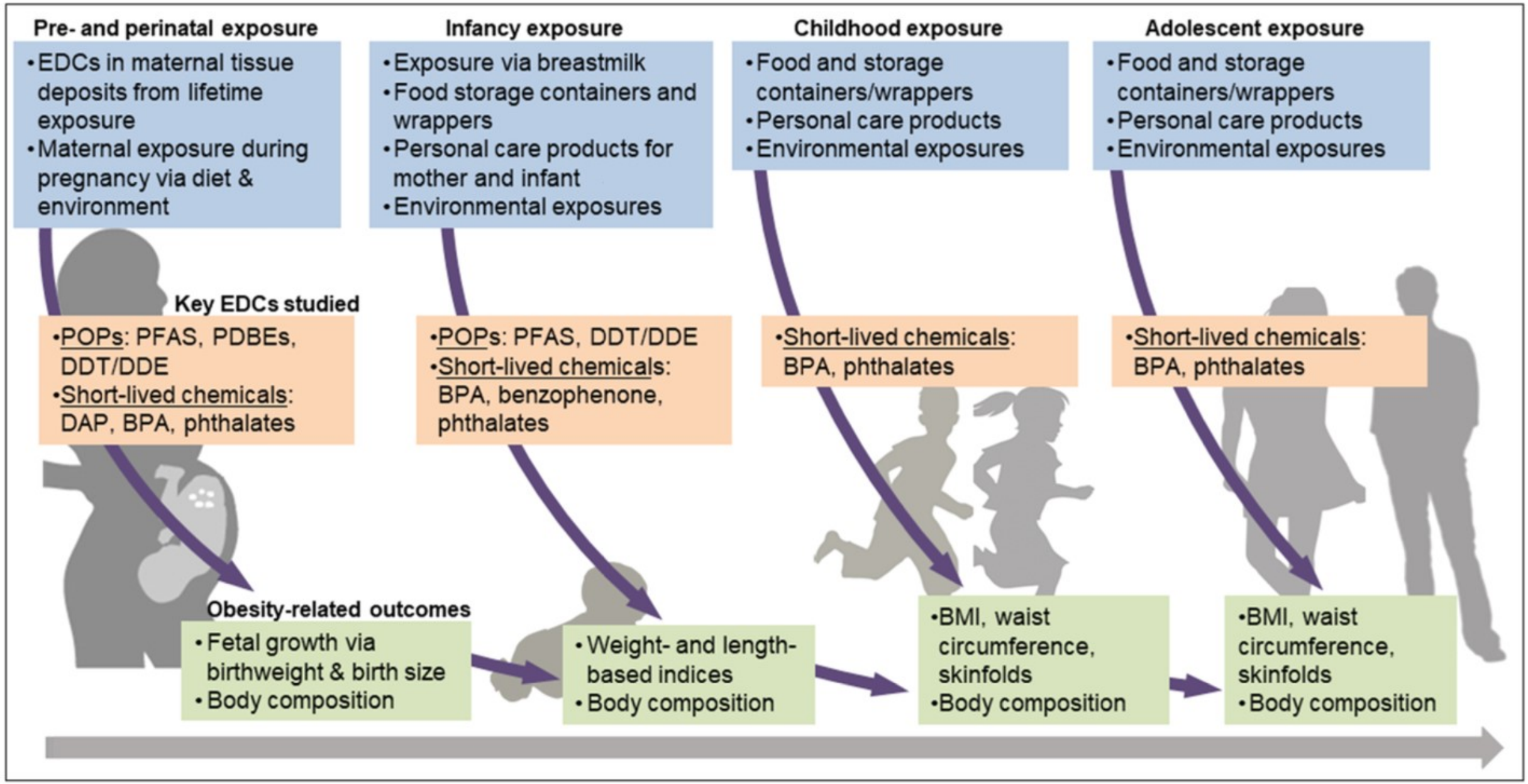
In Utero and Childhood Polybrominated Diphenyl Ether Exposures and Body Mass at Age 7 Years: The CHAMACOS Study

Ayca Erkin-Cakmak,[1] Kim G. Harley,[1] Jonathan Chevrier,[1,2] Asa Bradman,[1] Katherine Kogut,[1] Karen Huen,[1] and Brenda Eskenazi[1]

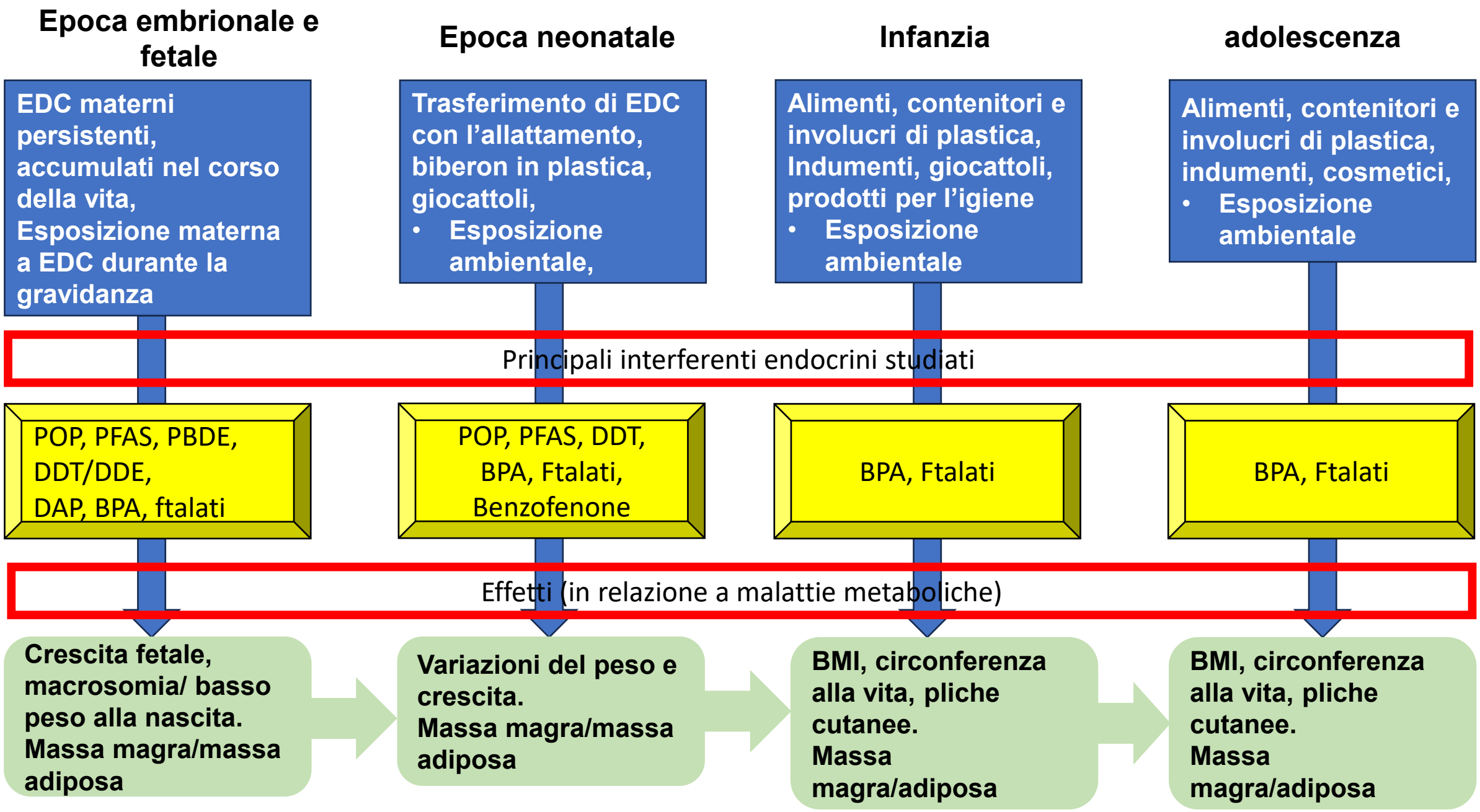
[1]Center for Environmental Research and Children's Health (CERCH), School of Public Health, University of California, Berkeley, Berkeley, California, USA; [2]Department of Epidemiology, Biostatistics and Occupational Health, McGill University Faculty of Medicine, Montréal, Québec, Canada

We estimated sex-specific associations with maternal PBDE levels during pregnancy and BMI at 7 years of age, finding positive associations in boys and negative associations in girls.

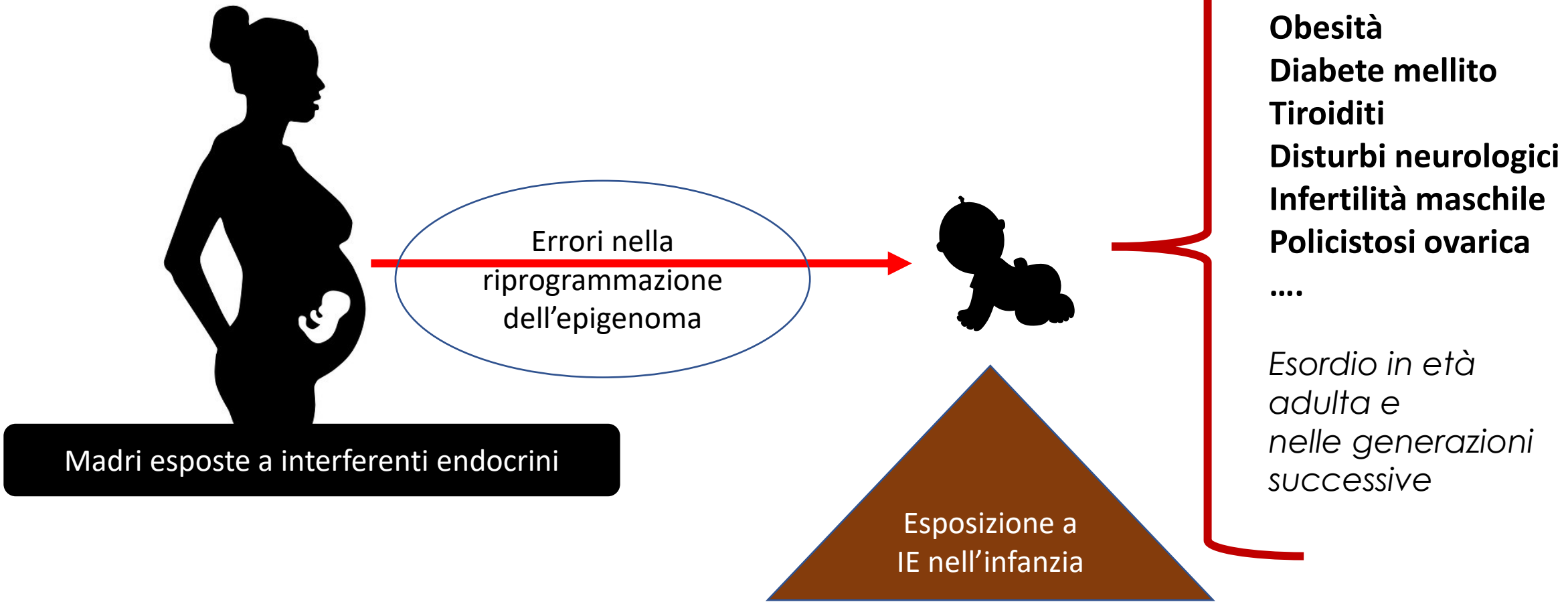
Environmental Health Perspectives, vol123 - n 6 - June 2015,



Obesity Reviews. 2021;22(S3):e13245.



Obesity Reviews. 2021;22(S3):e13245.


Madri esposte a interferenti endocrini
Errori nella riprogrammazione dell'epigenoma
Esposizione a IE nell'infanzia
Obesità
Diabete mellito
Tiroiditi
Disturbi neurologici
Infertilità maschile
Policistosi ovarica
….
Esordio in età adulta e nelle generazioni successive

Environment International 125 (2019) 58–64

Contents lists available at ScienceDirect

Environment International

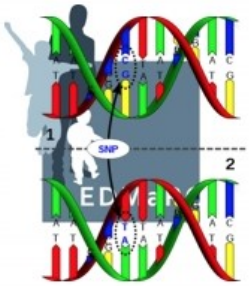
journal homepage: www.elsevier.com/locate/envint

Ambient air pollution and overweight and obesity in school-aged children in Barcelona, Spain

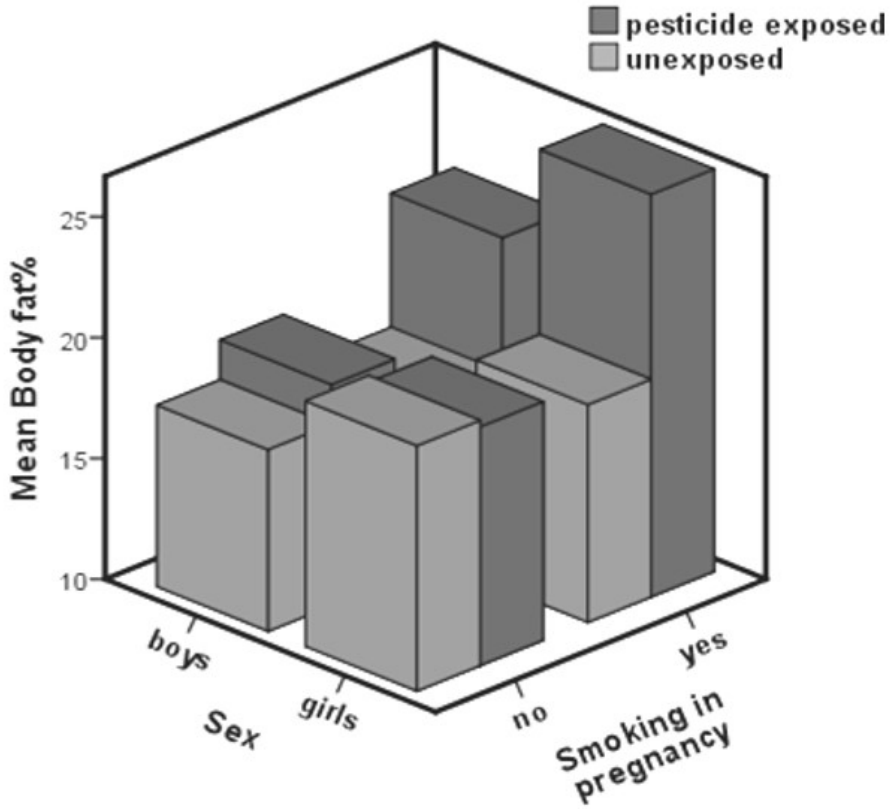
Jeroen de Bont[a,b,c], Maribel Casas[a,b,c], Jose Barrera-Gómez[a,b,c], Marta Cirach[a,b,c], Ioar Rivas[d], Damaskini Valvi[e], Mar Álvarez[a,b,c], Payam Dadvand[a,b,c], Jordi Sunyer[a,b,c], Martine Vrijheid[a,b,c,*]

[a] ISGlobal, Barcelona Institute for Global Health, Spain
[b] Universitat Pompeu Fabra (UPF), Barcelona, Spain
[c] CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain
[d] MRC-PHE Centre for Environment & Health, Environmental Research Group, King's College London, SE1 9NH London, United Kingdom
[e] Department of Environmental Health, Harvard T.H. Chan School of Public health, Boston, MA, United States

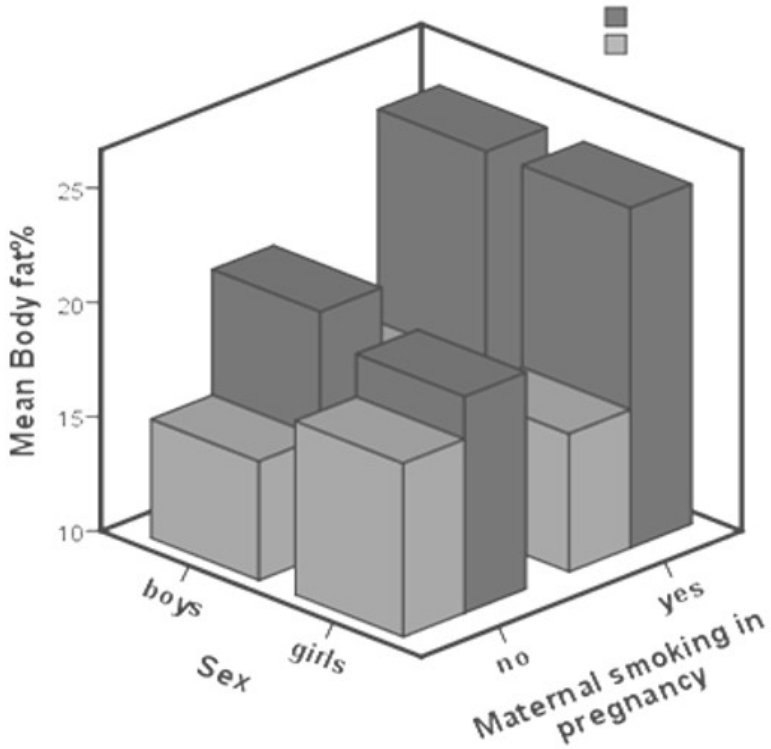
416'955 bambini tra 2 e 5 anni dell'area di Barcellona, seguiti dal 2006 al 2016: 142'590 (34,2%) sono diventati obesi o in sovrappeso. L'esposizione a polveri sottili e ad NO2 era associata ad aumento del 2-3% del rischio di sviluppare sovrappeso e obesità. Il rischio era più elevato nelle zone povere dell'area studiata.



All



PON1 R-allele



Tre fattori:

- **Predisposizione genetica**
- **Esposizione a pesticidi**
- **Madre fumatrice**

Increased blood pressure, HbA1c, leptin, DXA fat% in puberty

Andersen 2012, 2016, 2018; Tinggaard 2016; Jørgensen 2016; Declerck 2017

PON1 = paraoxonasi1

SICKER FATTER POORER

THE URGENT THREAT OF
HORMONE-DISRUPTING CHEMICALS
ON OUR HEALTH AND FUTURE . . .
AND WHAT WE CAN DO ABOUT IT

LEONARDO TRASANDE, M.D., M.P.P.

Consistenza delle prove di relazione causale tra specifici EDC e Diabete m. tipo 2				
	EDC	*Nell'Uomo*	*In vivo*	*In vitro*
Non persistenti	BPA	forte	Forte	Forte
	Sostituti di BPA	Dati insuff.	Dati insuff.	Dati insuff.
	Ftalati	contradditoria	bassa	forte
	arsenico	bassa	forte	forte
Persistenti	PCB	Forte	Forte	Forte
	PFAS (PFOA)	Bassa (forte per GDM)	bassa	bassa
	Diossine	forte	forte	forte
	DDT/DDE	forte	forte	forte
	TBT	bassa	possibile	bassa

C. Hinault et al – Int. J. Mol. Sci. - 2023 (24, 4573)

EDC e Diabete Gestazionale		
EDC	Meccanismi d'azione	Effetti sulla gravidanza
BPA	- PPARγ (alterazione del complesso recettoriale) - Effetto pro-infiammatorio - Inibizione del trasporto di glucosio - Attivazione ERβ	1. Aumento ponderale 2. Insulinoresistenza 3. ↑Adipogenesi 4. Disfunzione beta-cellulare 5. Alterazione dell'omeostasi glucidica
Parabeni	- PI3K-AKT (Interferenza con complesso recettoriale) - aumento stress ossidativo - interferenza con ormoni tiroidei	
Ftalati	- PPARγ (…) - PI3K-AKT (…)	
PFAS	- PPARγ (…) - interferenza con ormoni tiroidei	
Metalli pesanti (As, Cd, Hg)	. PPARγ (…) . attività proinfiammatoria	
Diossine	- PI3K-AKT (…) - attività proinfiammatoria (via AHR) - inibizione del trasporto di glucosio - stress ossidativo	
T.Mitra et al. Diabetology & Metabolic Syndrome (2024)		

Progetti europei (European Cluster on Identification of Endocrine Disruptors) – EURION -

EDC rapporti con:

- **OBESITA',**
- **DIABETE MELLITO TIPO II**
- **NAFLD**

GOLIATH

OBERON

EDCMET

Colture cellulari per rilevare interferenza con **attività ormonale tiroidea**

ATHENA

ERGO

SCREENED

Modalità di azione di EDC e **Sistema Neuroendocrino**

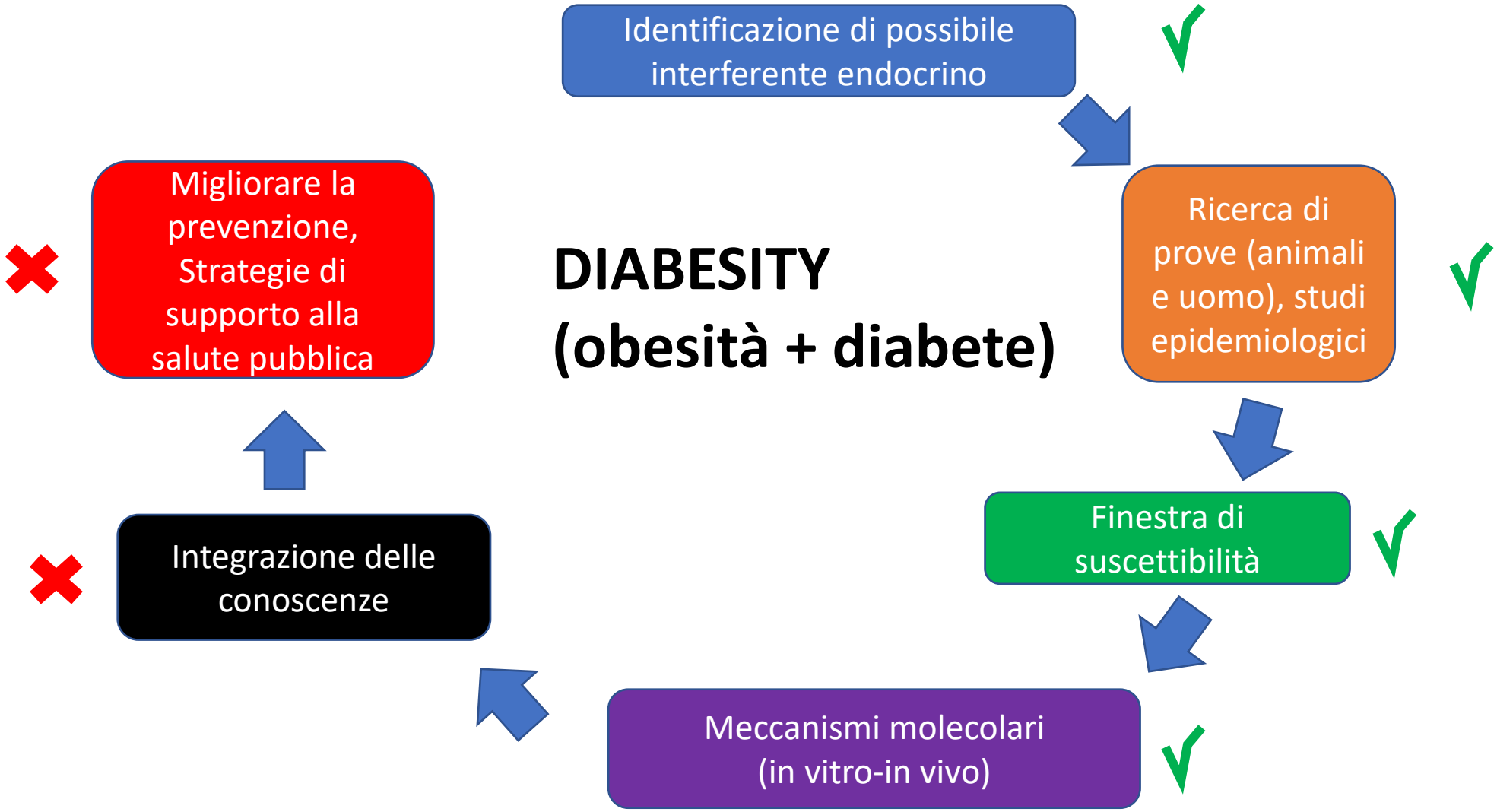
ENDpoiNTs

EDC e rapporti con **PCOS e fertilità femminile**

FREIA

Inserm

La science pour la santé
From science to health



Paloma Alonso-Magdalena - 2022 ECE
Miguel Hernandez University
Oberon Project - European Commission

Int.J.Mol.Scie. 23;21(8):2988

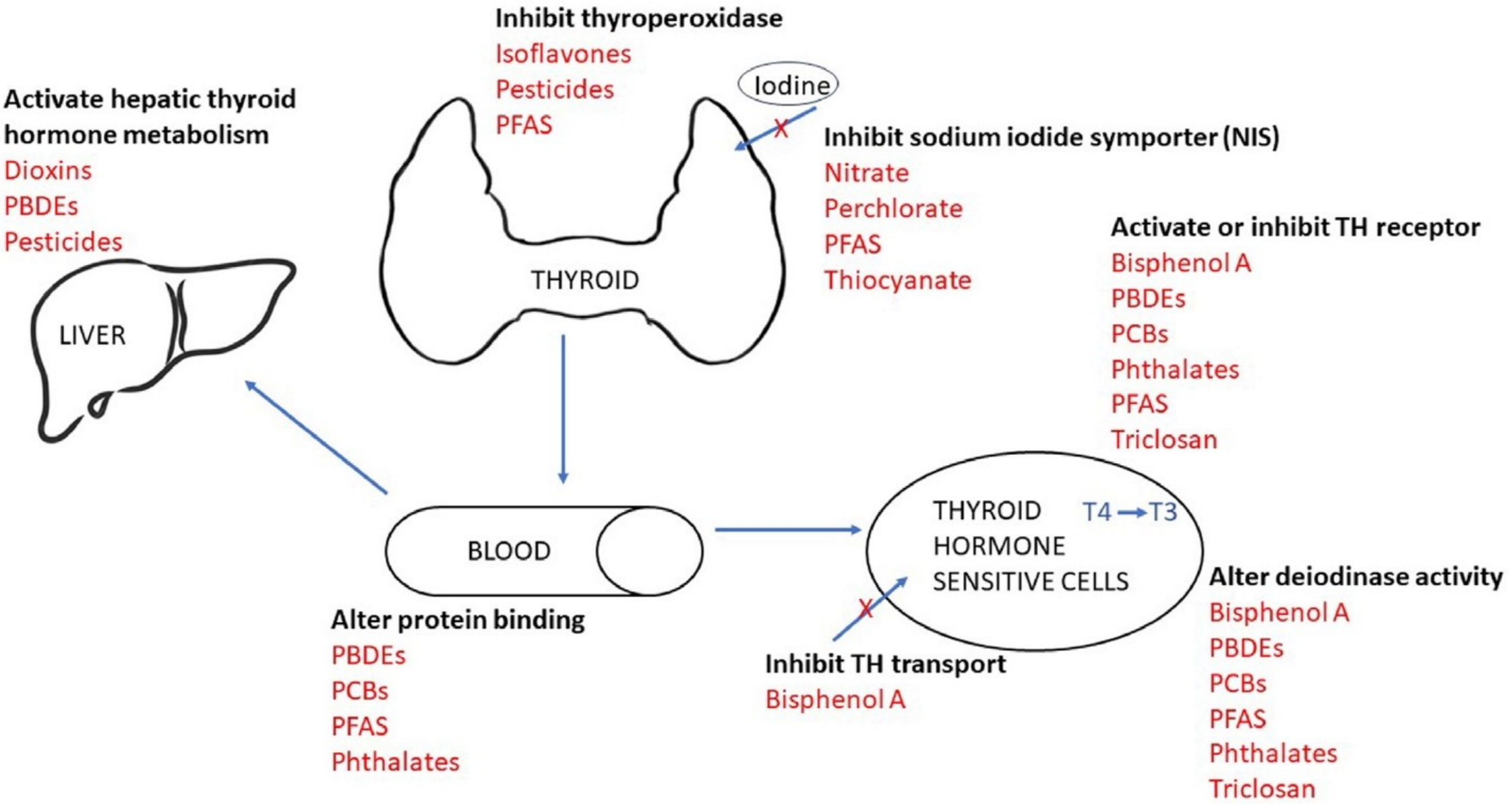
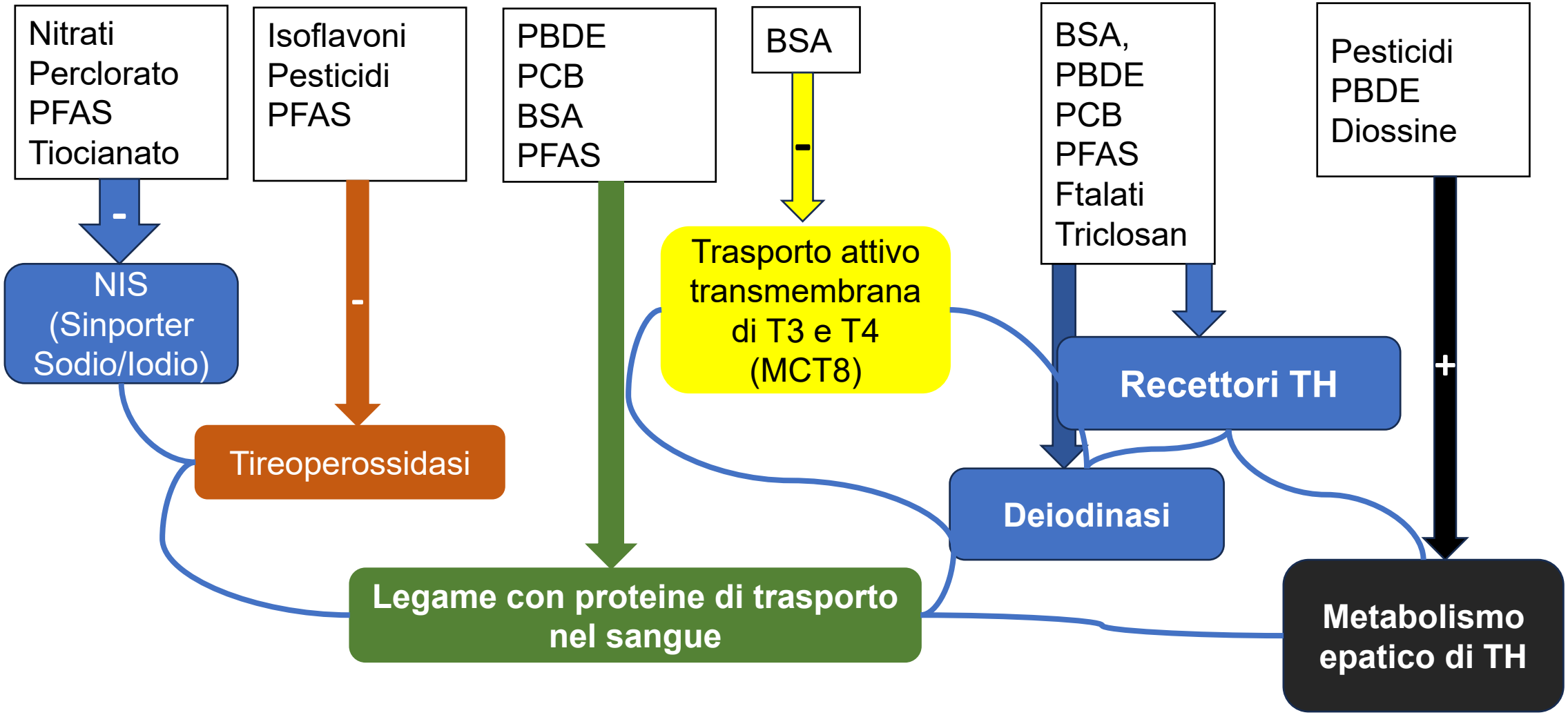


Fig. Effects of selected environmental thyroidal disruptors. *PBDE* = polybrominated diphenyl ether; *PCB* = polychlorinated biphenyl; *PFAS* = per- and polyfluoroalkyl substances; *TH* = thyroid hormone.

Endocrine Practice 30 (2024) 172e176

EDC e tiroide: modalità d'azione



Da: E.N.Pearce - Endocrine Disruptors and Thyroid Health - Endocrine Practice 30 (2024) 172e176

Allan-Herndon-Dudley syndrome (AHDS)

ATHENA Project

Toxicology in Vitro 96 (2024) 105770

Contents lists available at ScienceDirect

Toxicology in Vitro

journal homepage: www.elsevier.com/locate/toxinvit

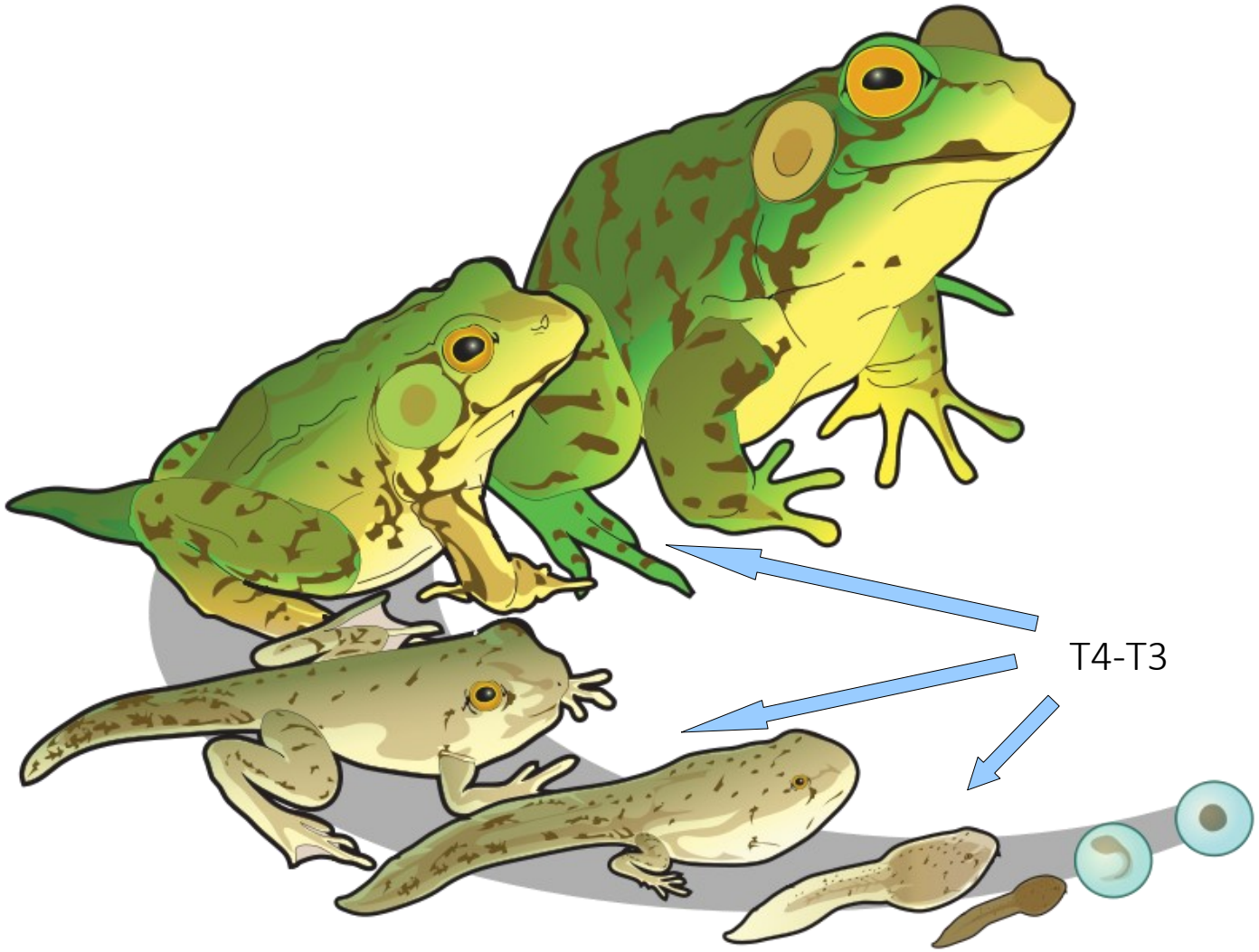
Screening for endocrine disrupting chemicals inhibiting monocarboxylate 8 (MCT8) transporter facilitated thyroid hormone transport using a modified nonradioactive assay

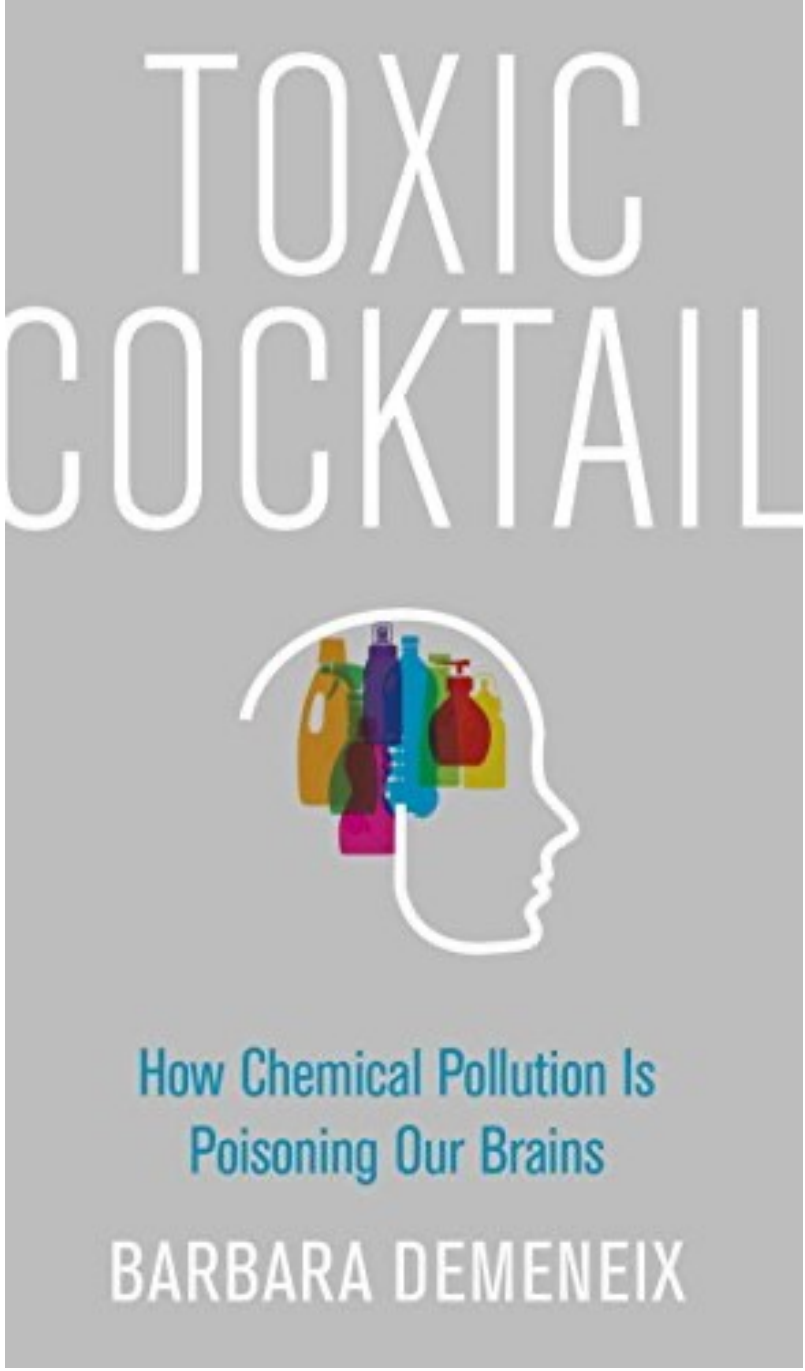
Fabian Wagenaars [a], Peter Cenijn [a], Martin Scholze [b], Caroline Frädrich [c], Kostja Renko [d], Josef Köhrle [c], Timo Hamers [a,*]

[a] Amsterdam Institute for Life and Environment (A-Life), Vrije Universiteit Amsterdam (VU), De Boelelaan 1085, 1081, HV, Amsterdam, the Netherlands
[b] Brunel University London, Centre for Pollution Research and Policy, College of Health, Medicine and Life Sciences, Kingston Lane, Uxbridge UB8 3PH, UK
[c] Charité – Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin Institut für Experimentelle Endokrinologie, Hessische Strasse 3-4, 10115 Berlin, Germany
[d] German Centre for the Protection of Laboratory Animals (Bf3R), Bundesinstitut für Risikobewertung (BfR), Berlin, Germany

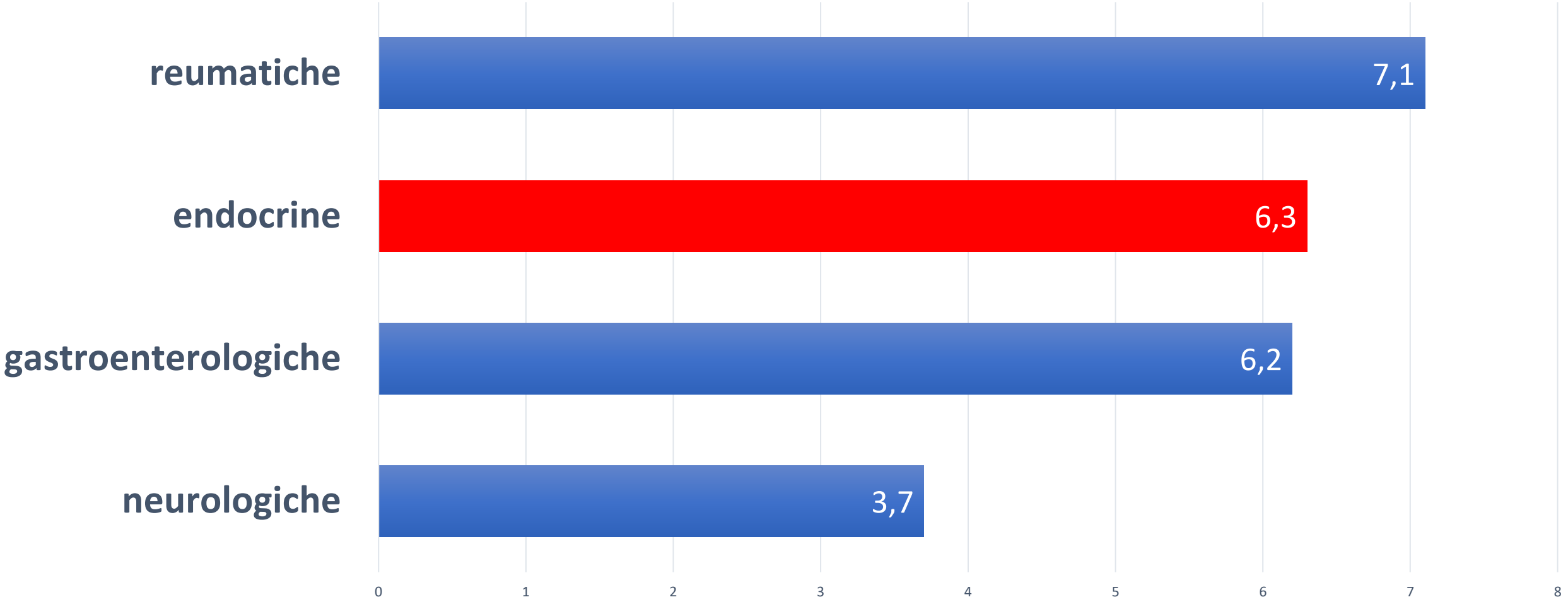
This alternative assay identified three novel MCT8 inhibitors:
methylmercury,
bisphenol-AF and
bisphenol-Z and
confirmed previously known MCT8 inhibitors [NB.: Verapamil, BSA, sunitinib]

BSA + pesticidi + PBDE





Malattie autoimmuni
aumento % annuale incidenza e prevalenza
1985 - 2015



A.Lerner- Int.J.Celiac Disease 2015

EDC	Sistema recettoriale/enzimatico	Interazione immunologica
BPA	MCT-8, TRα1, TRβ1	Alterata sintesi citochine
Ftalati	T3dT	Aumento iNOS e NFκB
Mercurio	Selenoproteine, deiodinasi	Aumento NET ed espressione TLR
PBDE	NIS, deiodinasi	Aumento citochine proinfiammatorie
Pesticidi (maneb/mancozeb, glifosato)	T3dT	Interferenza con recettori nucleari

T3dT = trascrizione/traduzione geni T3-dipendenti
MCT-8 = monocarboxylate transporter 8; TRα1,TRβ1= Recettori nucleari per l'ormone tiroideo α1 e β1;
NIS= symporter sodio/iodio; DIs= Desiodasi 1,2 e 3
iNOS = sintasi inducibile del monossido di azoto;
NFκB: nuclear factor kappa-light-chain- enhancer of activated B cells;
NET = Neutrophil Extracellular Traps
TLR = recettori Toll-like.

da: Il Cesalpino 2021 (52): 24-29

Environmental Science and Pollution Research (2022) 29:32882–32893
https://doi.org/10.1007/s11356-021-18110-0

RESEARCH ARTICLE

Quantifiable urine glyphosate levels detected in 99% of the French population, with higher values in men, in younger people, and in farmers

Daniel Grau[1] · Nicole Grau[1] · Quentin Gascuel[1] · Christian Paroissin[2] · Cécile Stratonovitch[3] · Denis Lairon[4] · Damien A. Devault[5] · Julie Di Cristofaro[6]

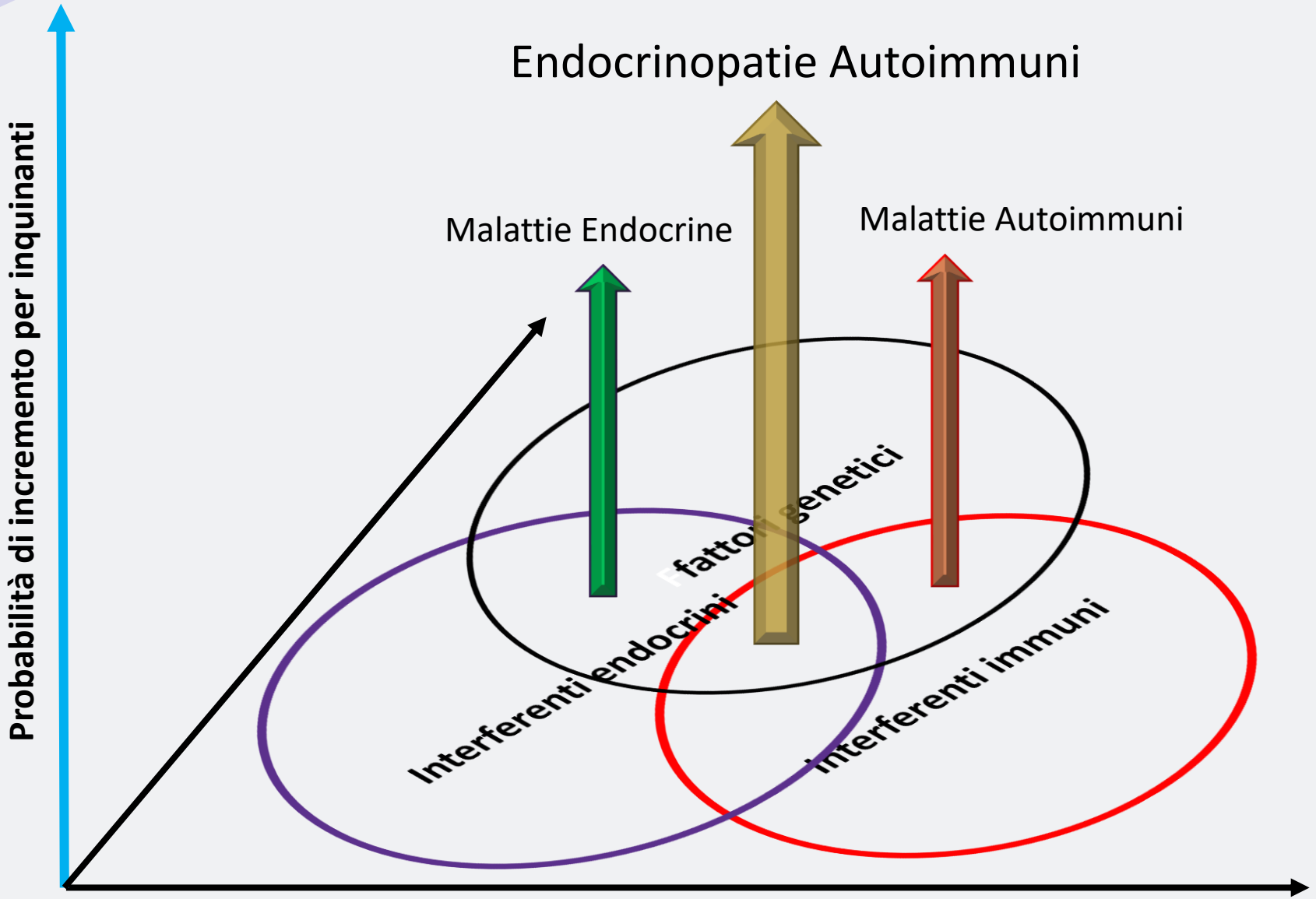
Received: 23 July 2021 / Accepted: 10 December 2021 / Published online: 12 January 2022

Review

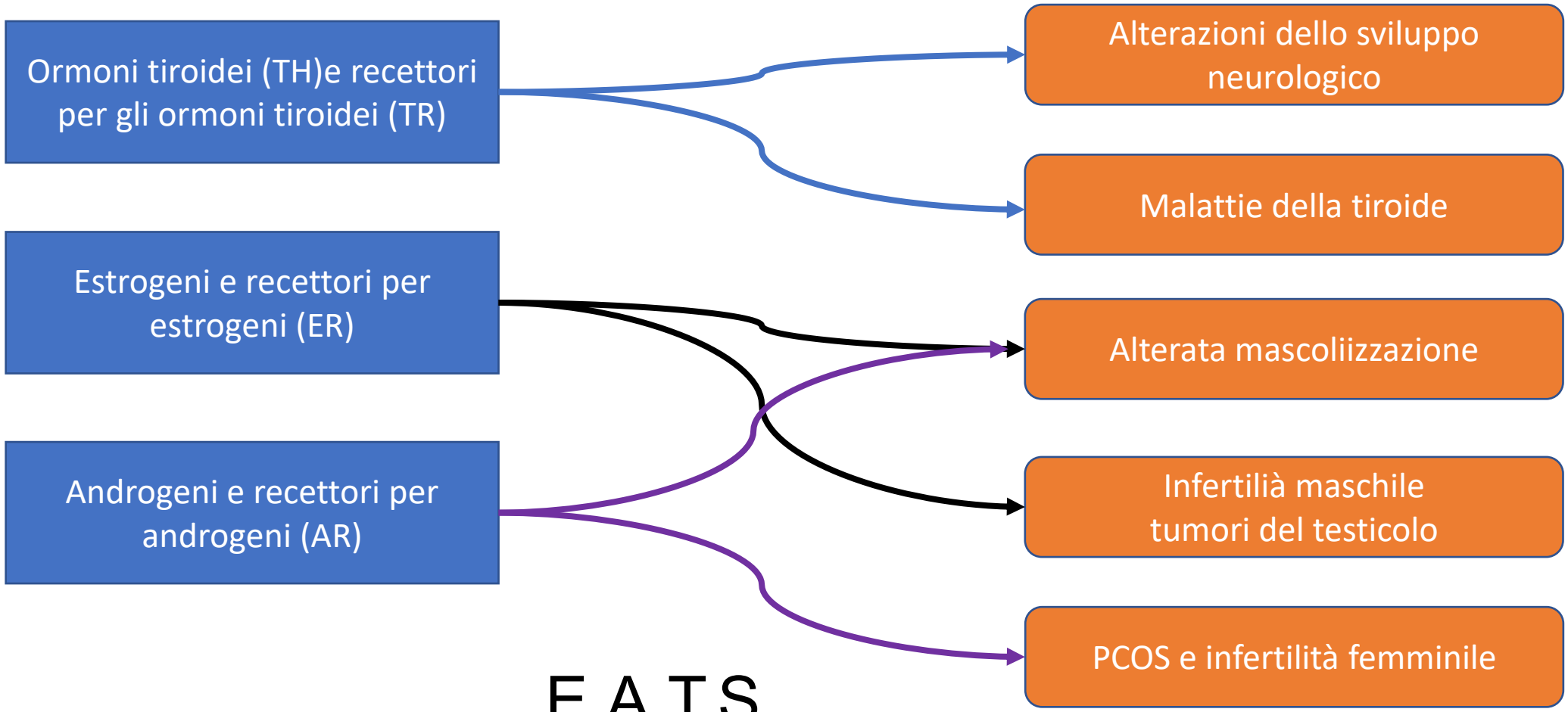
Review: Mechanisms of Glyphosate and Glyphosate-Based Herbicides Action in Female and Male Fertility in Humans and Animal Models

Loïse Serra [1], Anthony Estienne [1], Claudine Vasseur [2], Pascal Froment [1] and Joëlle Dupont [1,*]

Cells **2021**, *10*, 3079. https://doi.org/10.3390/cells10113079


Endocrinopatie Autoimmuni
Malattie Endocrine
Malattie Autoimmuni
Probabilità di incremento per inquinanti
Fattori genetici
Interferenti endocrini
Interferenti immuni

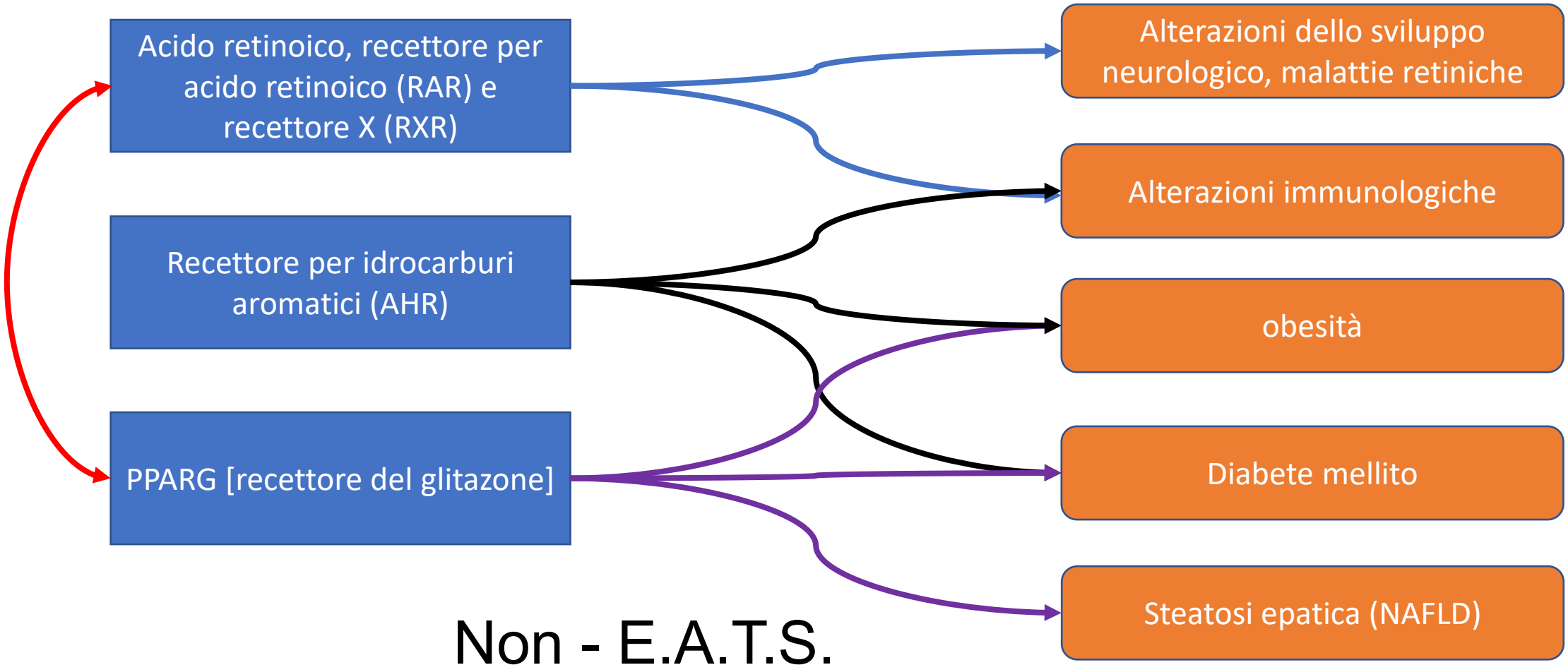
Sistemi endocrini per cui esistono dati consolidati



E.A.T.S.

Estrogeni-Androgeni-Tiroide-Surrene

Nuovi sistemi endocrini studiati



Non - E.A.T.S.