

ENDOCRINE SOCIETY



Hormone Science to Health

Identifying EDCs for Public Health Protection: The Endocrine Perspective

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Introduction

Over 18,000 members – rapidly growing

122 Countries, 40% from outside US

World's leading experts in Hormone Research

ENDOCRINE
SOCIETY





ACOG
THE AMERICAN COLLEGE
OF OBSTETRICIANS
AND GYNECOLOGISTS



Royal College of
Obstetricians
and Gynaecologists



World Health
Organization



American Chemical Society

EDCs are a global health threat

Diabetes

Metabolic

Neurobehavioral

Reproduction

Immune deficiencies

Birth Defects

IQ loss

Cancers

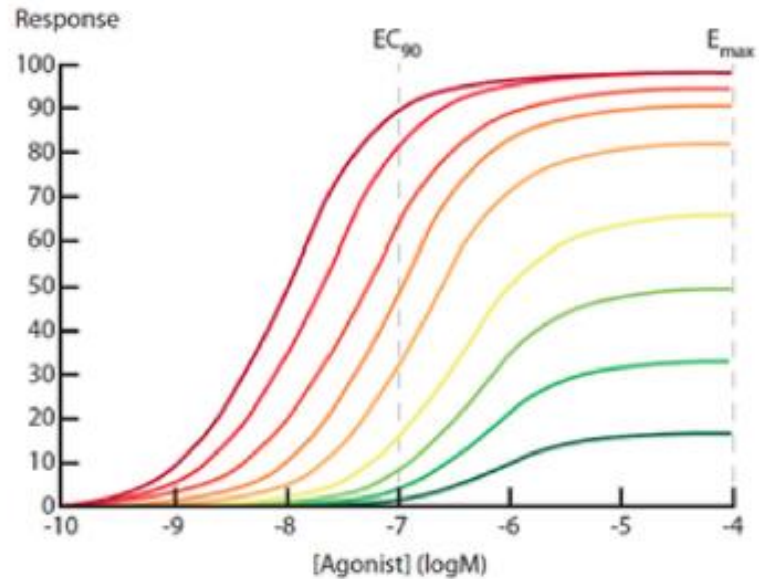
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Hormones:

- Act on receptors
- Control development
- Act at low concentrations

B



Receptor number (% total)



Critical features of hormone action

1. Outcome – population and individual level
Adverse = risk factors for chronic disease
2. Timing of exposure – defines outcome.
3. Permanence – effects are irreversible.

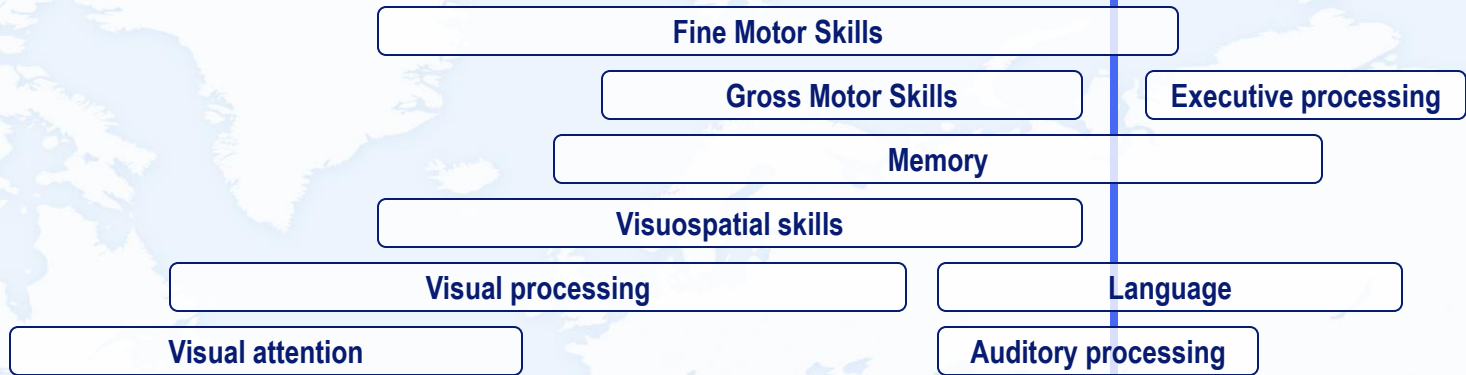
Thyroid Hormone and brain development:

Synthetic chemicals can interfere with thyroid hormone action in the developing brain without changing hormone levels in the blood.



HUMAN DEVELOPMENT

BIRTH



FIRST TRIMESTER	SECOND TRIMESTER	THIRD TRIMESTER	POSTNATAL
Thyroid Hormone		Brain Development	
G1-G17	G17-G21	POSTNATAL	

Callosal Projections

Gene expression
RC 3, NSP-A, Oct-1

Neuronal migration
Cortial lamination

Open field activity

Cerebellar granule cells
Granule cells proliferation
Granule cell migration to IGL
Granule cells apoptopsi

Purkinje cell maturation
MPB, RC 3, Reelin, Rhes

BIRTH

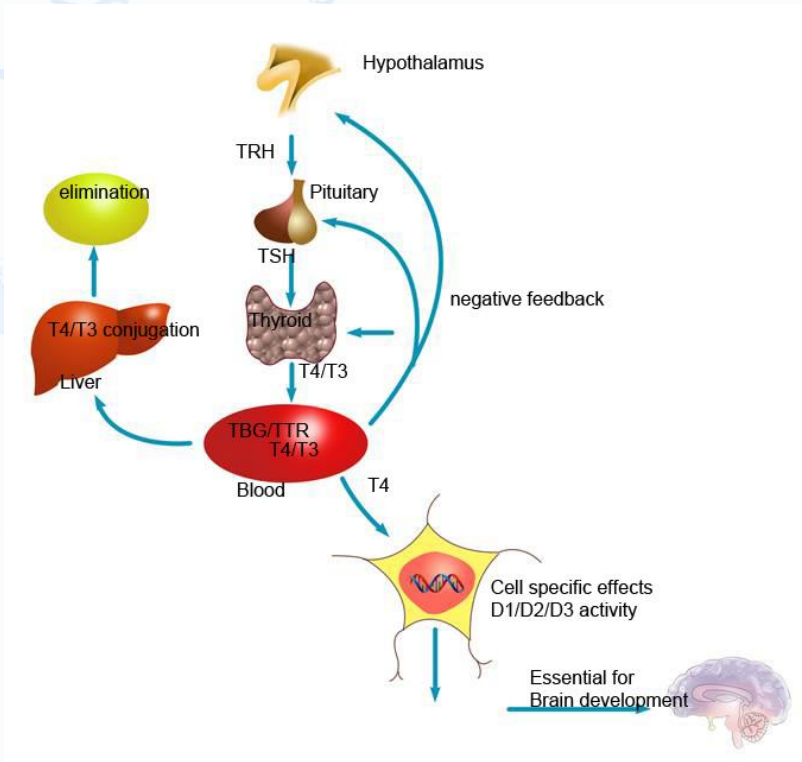
RODENT DEVELOPMENT

Zoeller & Rovet, 2004



Conclusions

- Thyroid hormone is important.
- But, no mammalian endpoints of TH action in current screens/tests
- No compensation



Thyroid is but one hormone system

- Gonad
 - Adrenal
 - Kidney
 - Pancreas
 -
- Muscle
 - Gut
 - Brain
 - Heart

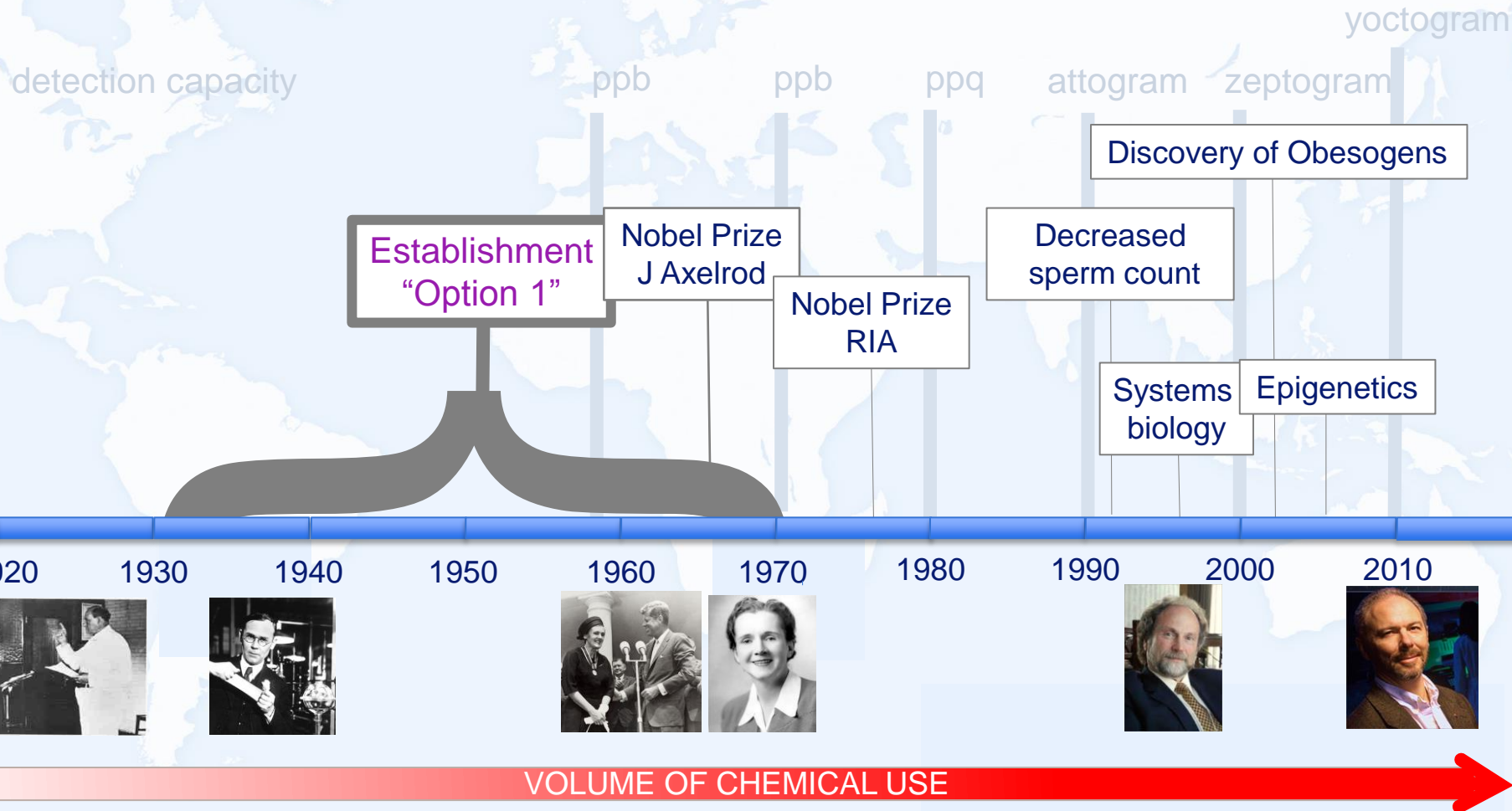


Endocrine Society favors “Option 3”

OPTION ONE

← Obsolete criteria

Criteria must derive from contemporary understanding of the endocrine system.



Endocrine Society favors “Option 3”

OPTION ONE

OPTION TWO

← One category only, unrealistic

Endocrine Society favors “Option 3”

OPTION ONE

OPTION TWO

OPTION THREE

← Several categories,
most rational approach



Endocrine Society does not agree with “Option 4”

OPTION ONE

OPTION TWO

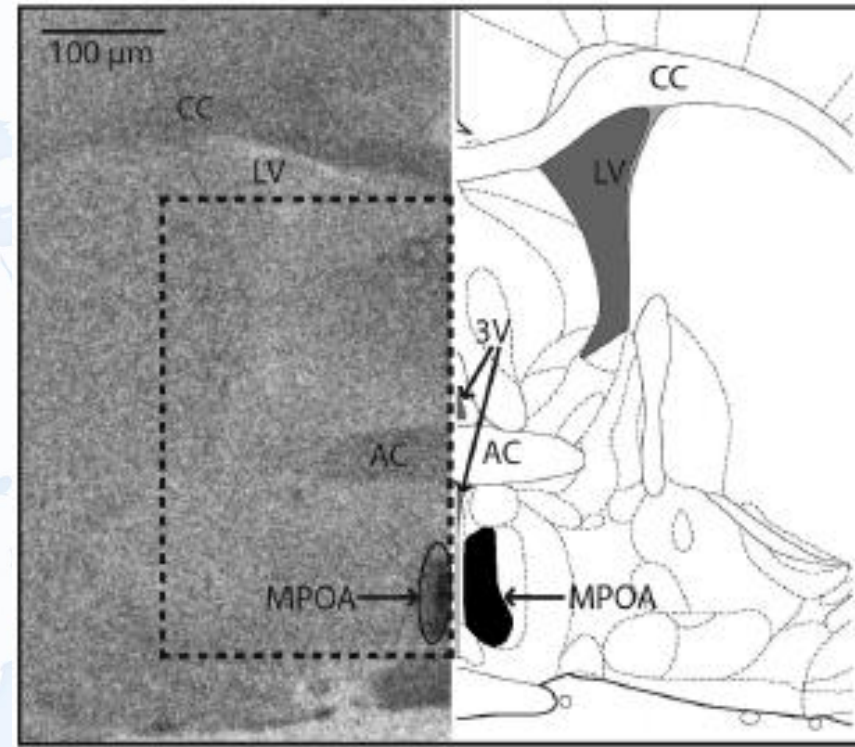
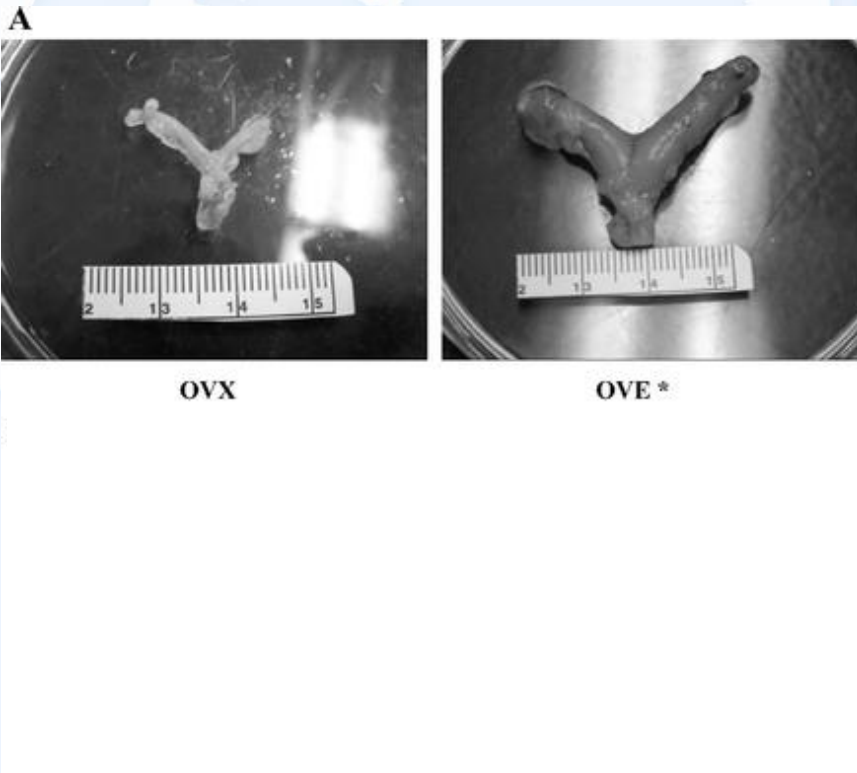
OPTION THREE

~~OPTION FOUR~~

Using potency cut off as a predominant factor would be a mistake



Why “Potency” as a cut-off is a Mistake



Rebuli ME, Cao J, Sluzas E, Delclos KB, Camacho L, Lewis SM, Vanlandingham MM, Patisaul HB. *Toxicol Sci.* 2014;140(1):190-203.
Delclos KB, Camacho L, Lewis SM, Vanlandingham MM, Latendresse JR, Olson GR, Davis KJ, et al. *Toxicol Sci.* 2014.

Endocrine Society favors “Option 3”

OPTION ONE

OPTION TWO

OPTION THREE

OPTION FOUR

Using potency cut off as a predominant factor would be a mistake



This is serious

- Current approach does not capture all EDCs
- Endocrine Perspective is critical
 - Specific endpoints
 - Low dose
 - No threshold
 - Adversity = risk factors
 - Use of the open literature
 - Estimated costs of endocrine-disrupting chemical exposure exceed €150 Billion annually in EU