Intervención Biomédica

¿El Autismo es prevenible , reversible y tratable?

Dr. Lorena Benarroch

Autismo

Complejo Desorden Multifactorial del desarrollo Neurológico (sindrome pervasivo del desarrollo)

Deficit de atención ***Autismo*** ***Asperger***

Un porcentaje alto de niños presentan contaminación con metales pesados

79% mejoran con quelación

¿Que es el Autismo?

Complejo desorden médico multifactorial del desarrollo (neurológico)

"lenguaje, socialización y conducta"

Cada niño con Autismo tiene anormalidades biológicas únicas que requieren intervención BIOMEDICA individualizada

Desorden *del* SNC ? ó Desorden que afecta *al* SNC ?

Emerge un nuevo modelo en Autismo verosimil, creible, y demostrable

Especificidad	Cambios locales	Daño disperso
Locus	SNC	Sistémico
Causa	Genética	Desencadenantes ambientales Susceptibilidad genética
Plasticidad	Cableado	Cambios metabólicos y estructurales
Pronóstico	Incurable	Tratable

Herbert MR.2005 Autism : A brain disorder or a disorder that affects the Brain? Clinical Neuropsychiatry 2:354-79

Evidencia emergente requiere un nuevo modelo de enfermedad

▪Raro, trágico, prevalencia constante ▪Complejas causas genéticas ▪Resultados determinados in útero ▪Neuro-genético	▪Alarmante aumento en frecuencia ▪Enfermedad ambiental posible vulnerabilidad genética ▪Eventos prevenibles ▪Problema multidisciplinario: toxicología, epidemiología, neurología, inmunología, gastroenterología
Tratamiento: conductual	Prevención, tratamiento, y recuperación

"Niños defectuosos"

"Nuestros niños estan enfermos"

Muchos expertos en Autismo, opinan:

- *No hay epidemia, diagnosticamos mejor!*
- *N*
- *N* *IC*
- *L*
- *Th* *as tóx* *para el hombre?”* *es realmente segura en las vacunas”*

Erick Honneker dijo que el muro de Berlin estaria 100 años mas!

Ya no existe!!!!!!!

Enfermedad

PRECIPITANTES

Tóxicos/biológicos/físicos /emocionales

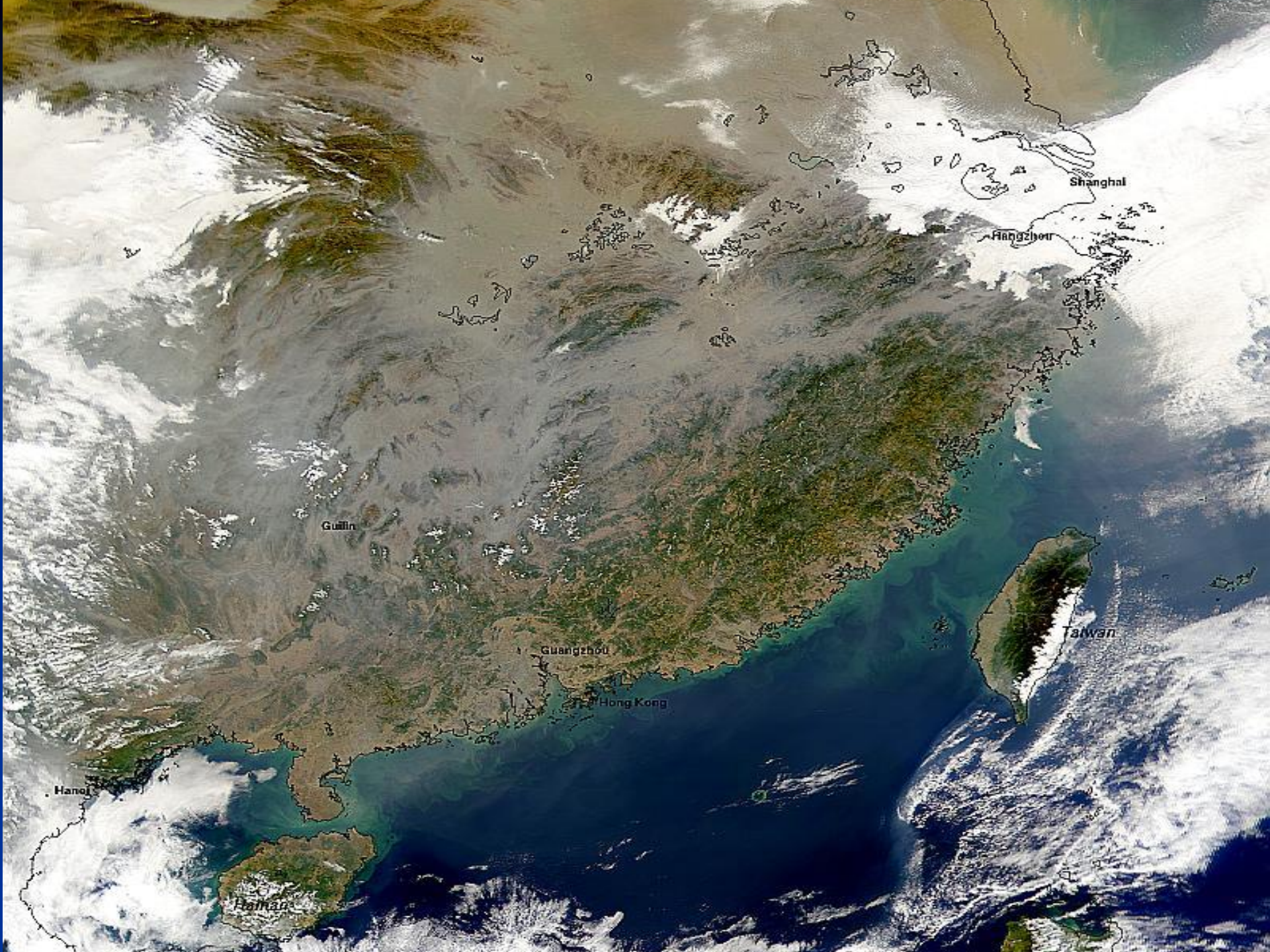
PERSISTENCIA

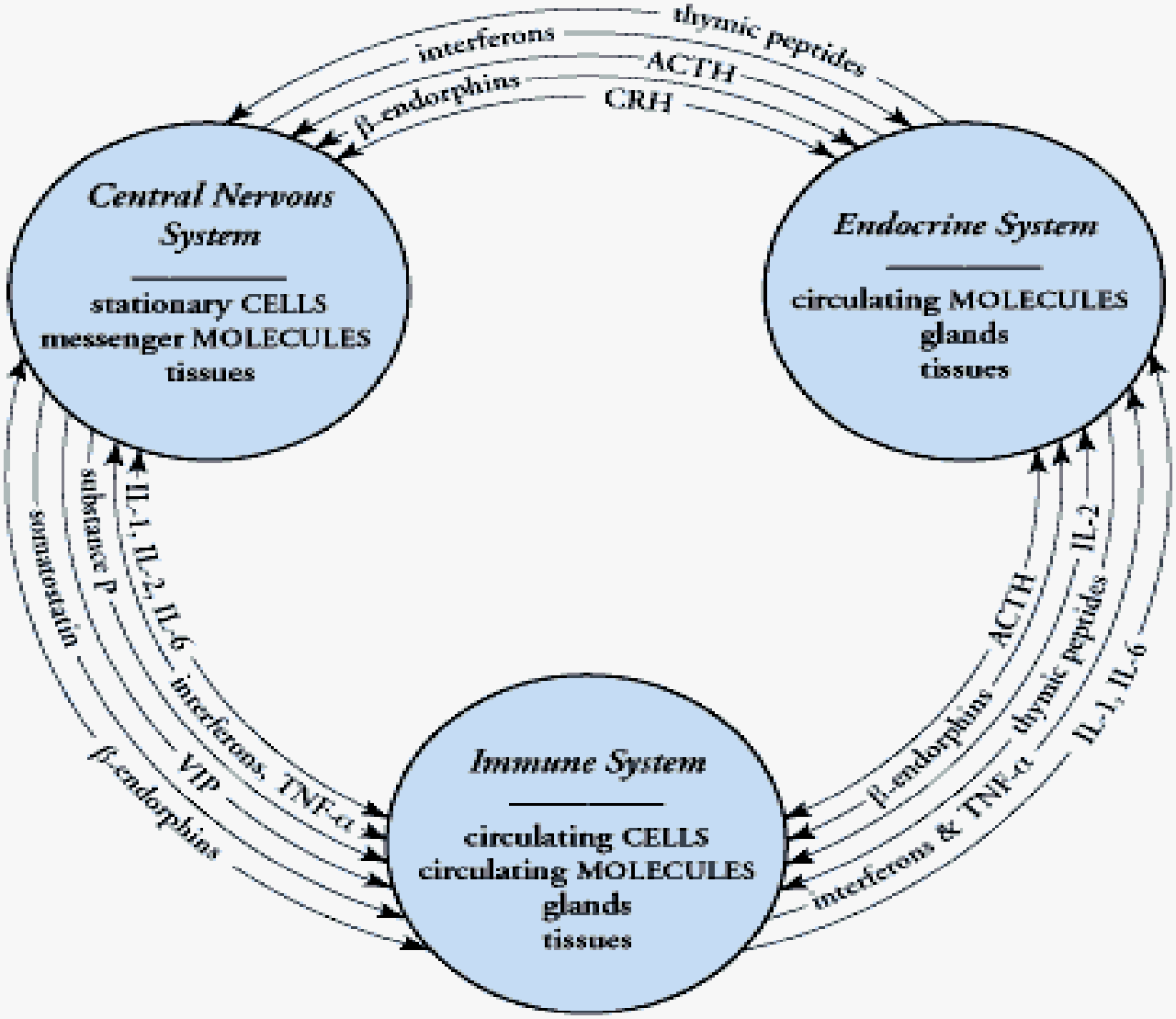
Ambiente/Estilo de Vida
Factores Psicológicos

PREDISPONENTES

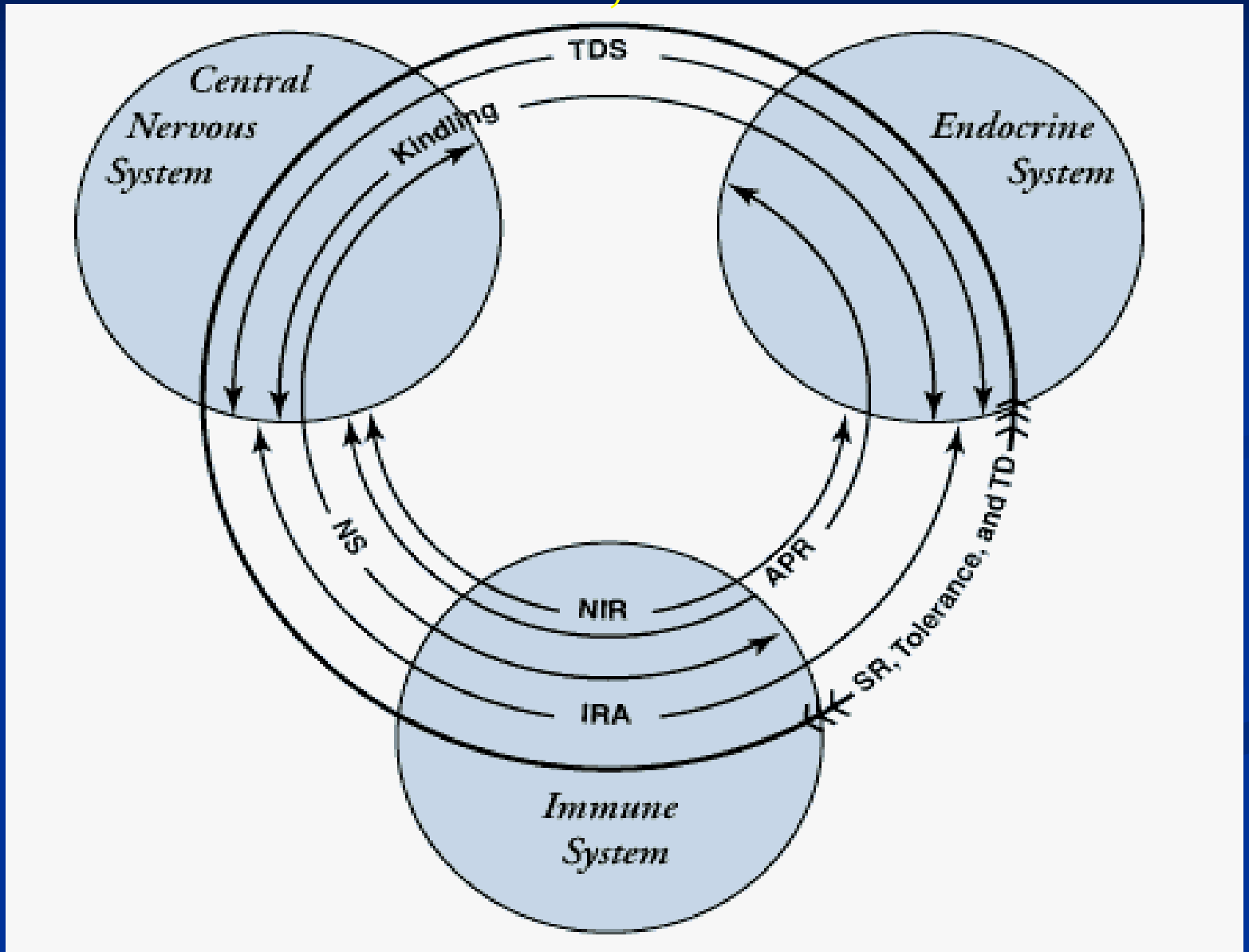
Genético/Adquirido

El niño se convierte en victima de su sistema inmune


Shanghai
Hangzhou
Guilin
Guangzhou
Hong Kong
Taiwan
Hanoi
Hainan

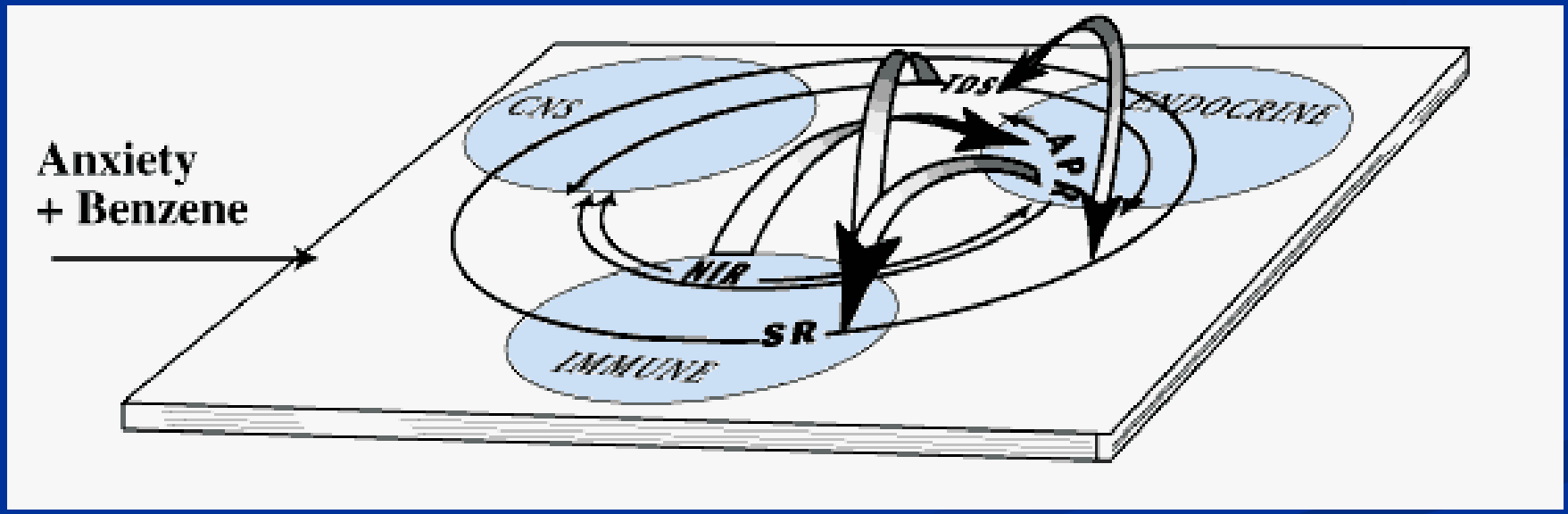

thymic peptides
interferons
ACTH
β-endorphins
CRH
Central Nervous System
stationary CELLS
messenger MOLECULES
tissues
Endocrine System
circulating MOLECULES
glands
tissues
IL-1, IL-2, IL-6
substance P
somatostatin
interferons, TNF-α
VIP
β-endorphins
ACTH
β-endorphins
IL-2
thymic peptides
IL-1, IL-6
interferons & TNF-α
Immune System
circulating CELLS
circulating MOLECULES
glands
tissues

Bencenos, Poluci☼n ambiente NO2,PBCs, Insecticidas, Pesticidas.

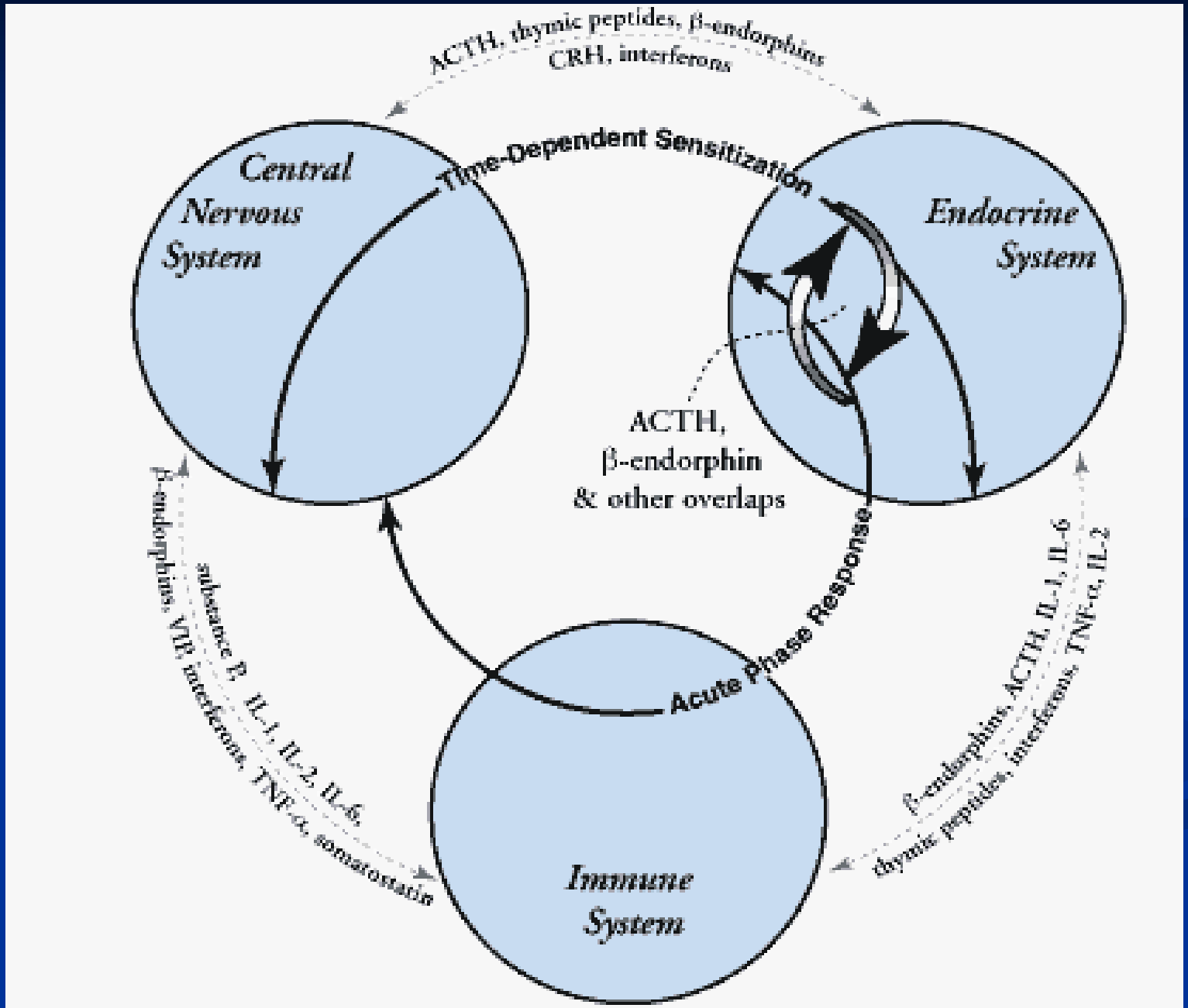


Sin importar cual es el desencadenante **CAOS !!!**

Imposibilita encontrar marcadores biológicos adecuados ***OJO***



Metales pesados?



"3 P's"

Predisponentes

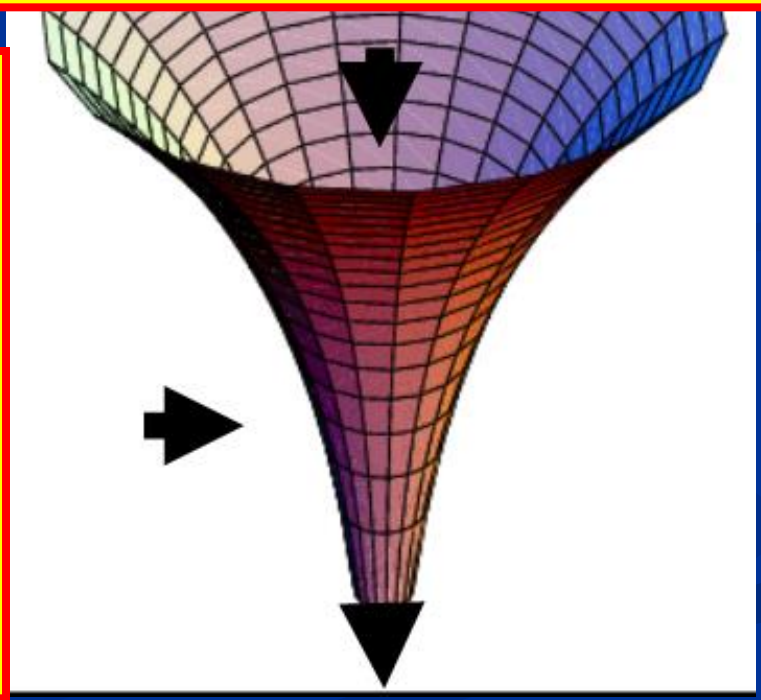
Debilidad congénita hacia retos del neurodesarrollo:

- **Genética-PKU,Fragil X, gemelos idénticos-75%**
- **Genetica:polimorfismos múltiples leves, auto inmunidad**
- ***Epigenetica:* exposición in-útero, infecciones, tóxicos,**
- **déficit nutricionales heredados**

Precipitantes

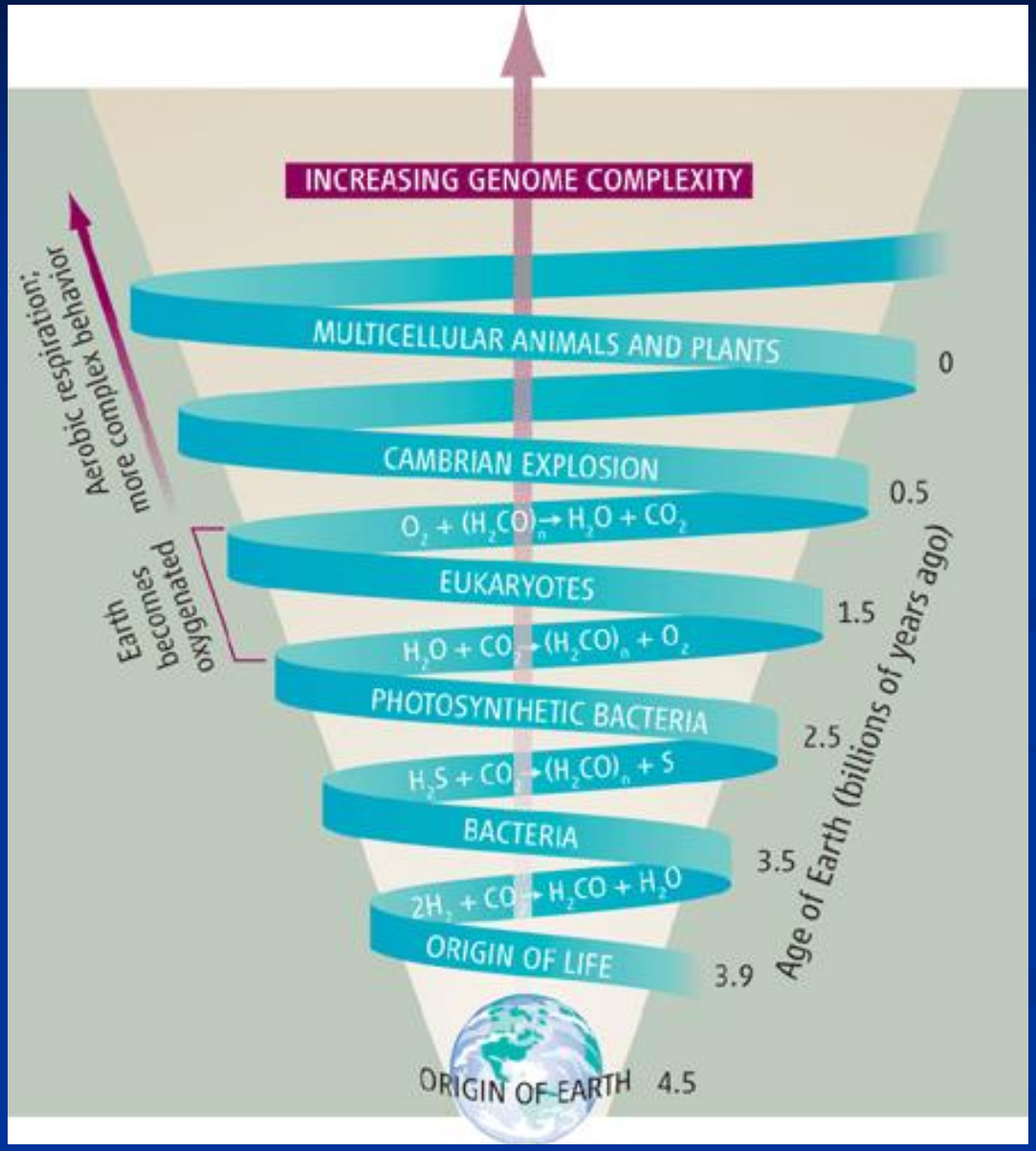
Stress Oxidativo, inflamación por:

- **Vacunas**
- **Medicamentos**
- **Exposición xenobiotica**
- **Deficiencias nutricionales**
- **Inmunidad, Infección, GI**



Persistencia causa incremento Espectro Autista

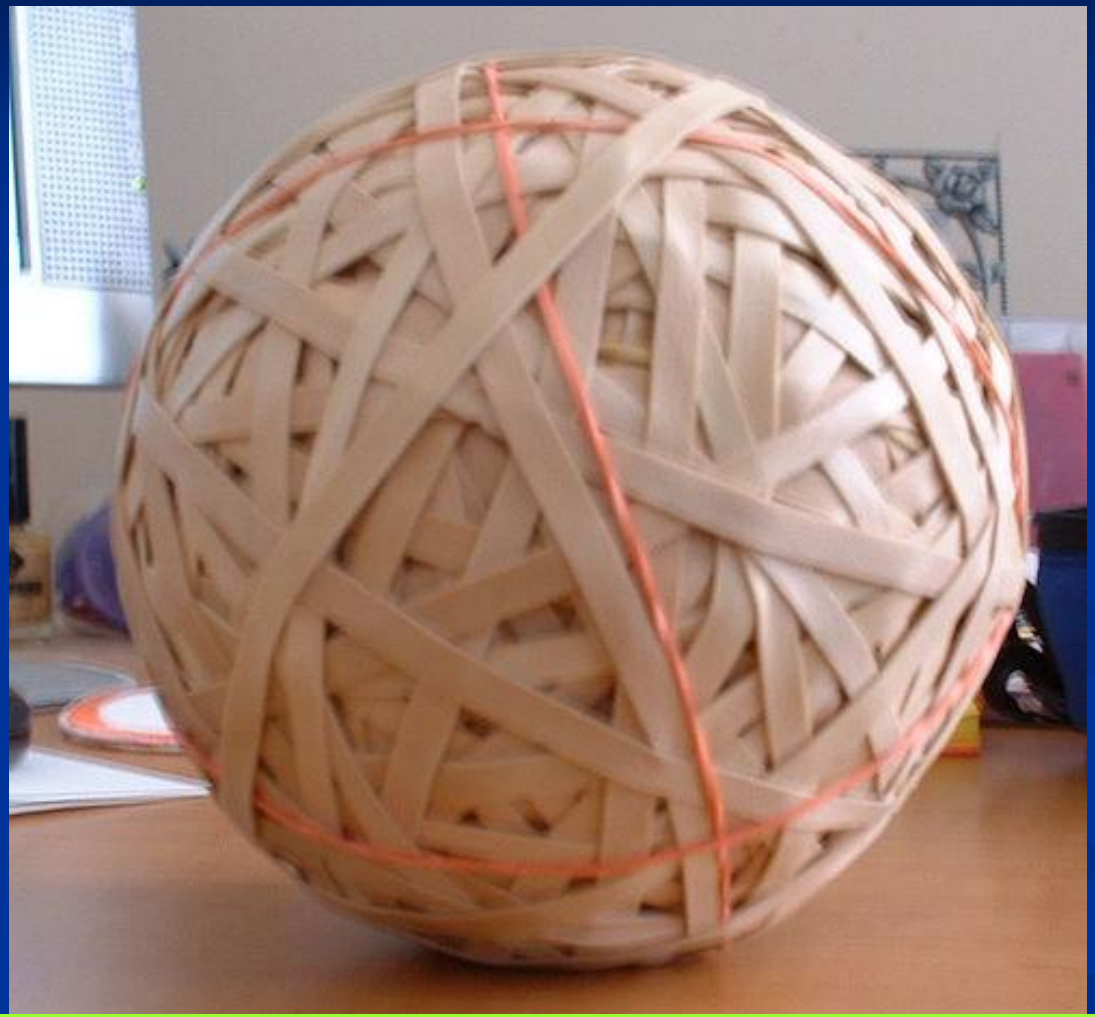
Evolución= adaptación metabólica al ambiente oxigeno



Δ Sulfur metabolism
+
Cobalamin synthesis
by selected bacteria

Figure from Paul G. Falkowski
***Science* 311 1724 (2006)**

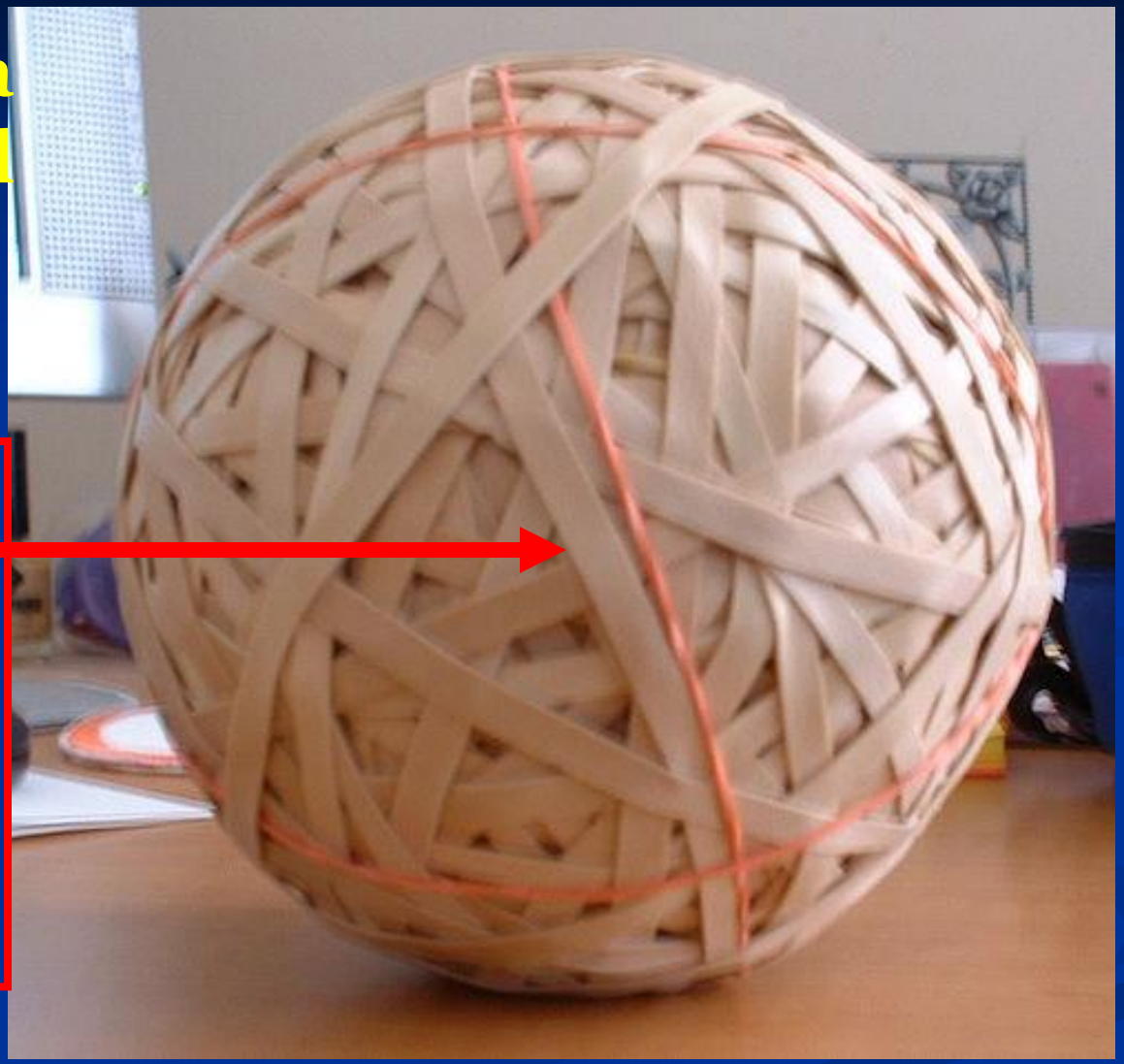
Evolucion: capas sobre capas de respuestas adaptativas al cambio ambiental



Richard Deth, PhD Northeastern University Boston, MA. Autism One 2008

La habilidad de controlar la oxidación es el corazón de la evolución

Cada adición se refuerza porque se construye sobre un corazón solido!



Richard Deth, PhD Northeastern University Boston, MA. Autism One 2008

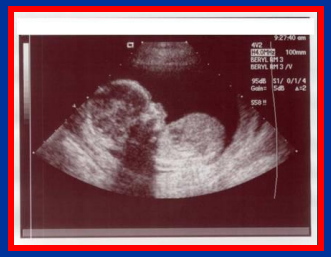
Nuevas capacidades se agregan en el contexto del ambiente

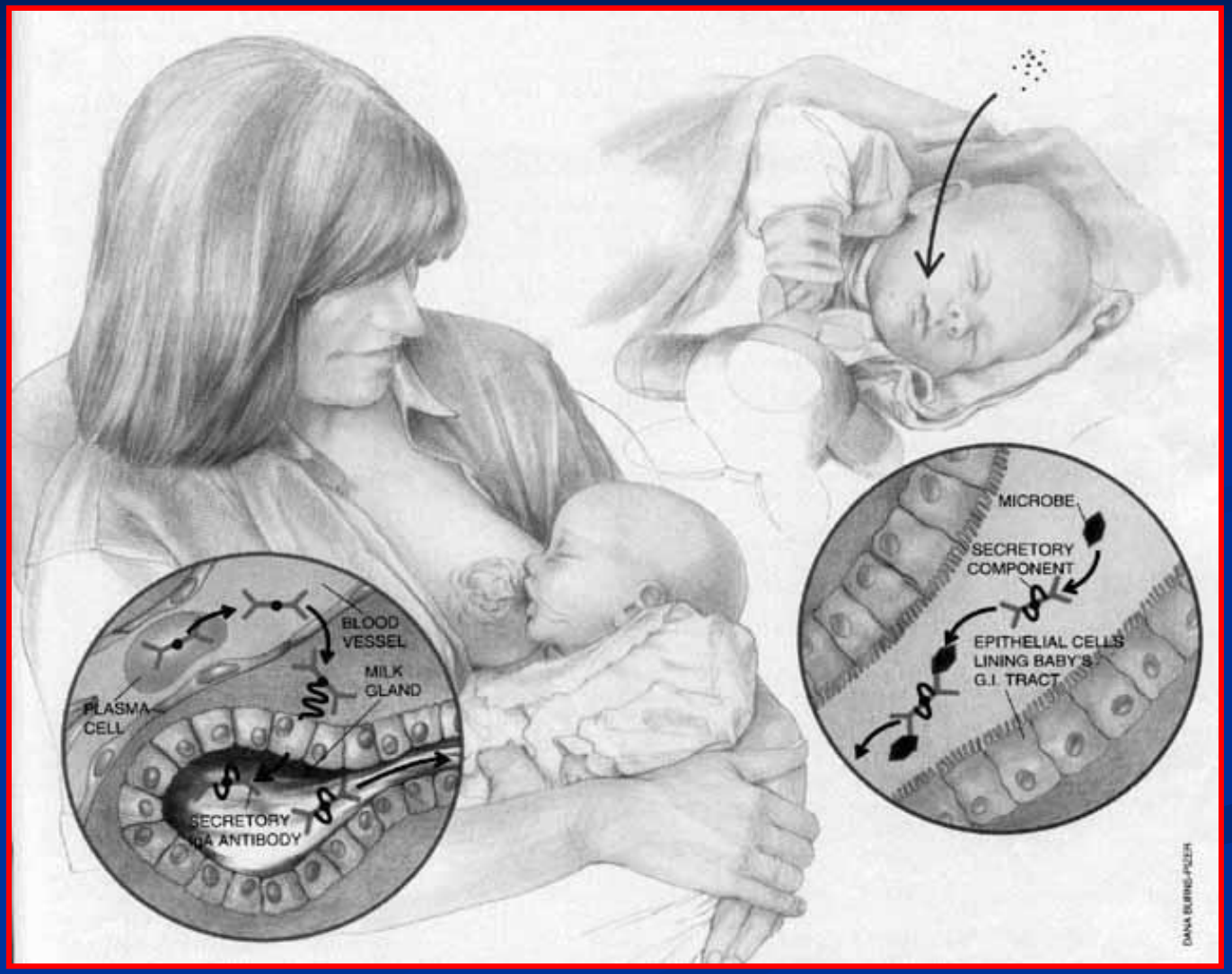
Capacidades añadidas recientemente son las mas vulnerables, de perderse cuando hay cambios significativos en el ambiente

Las capacidades cognitivas del humano son particularmente vulnerables

Richard Deth, PhD Northeastern University Boston, MA. Autism One 2008

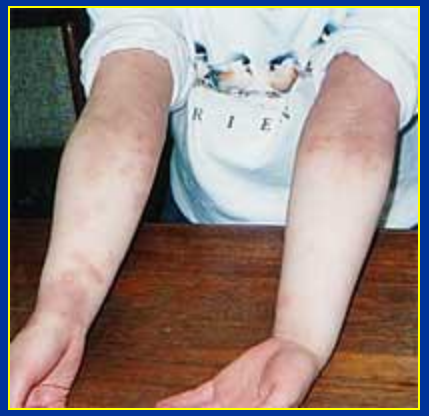
Inmunomodulación



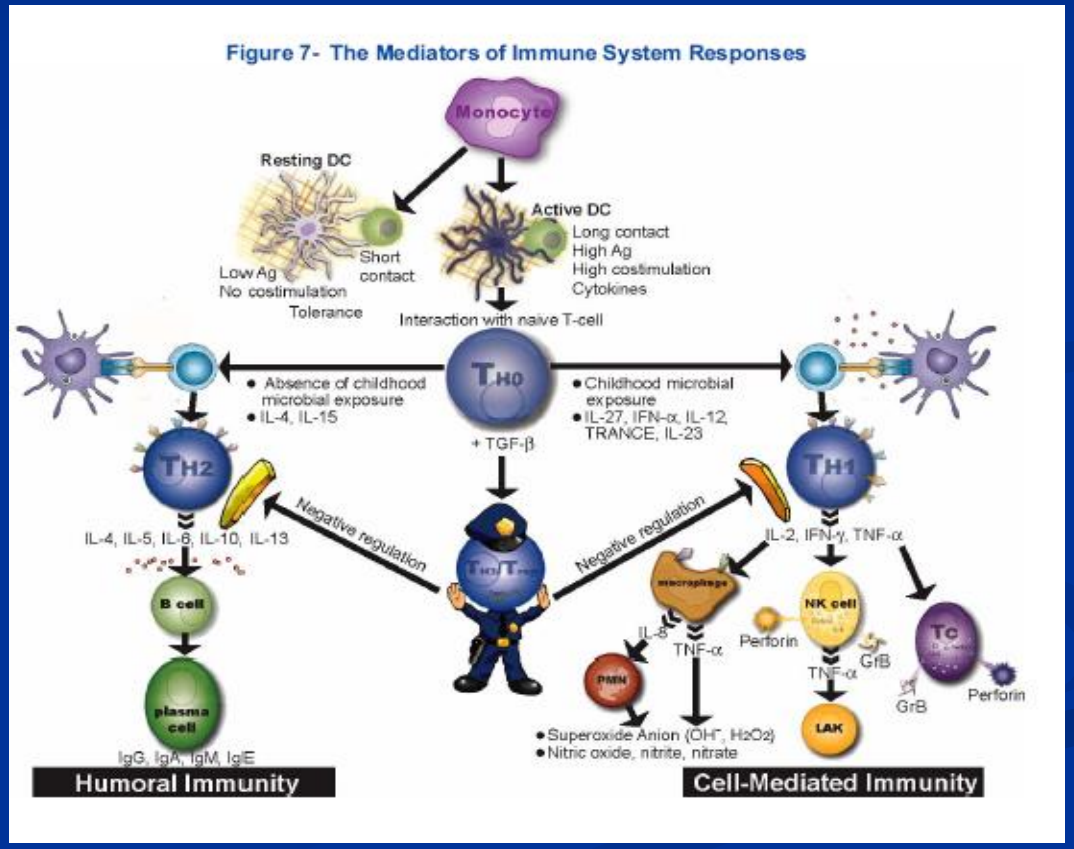


Enfermedad: Sistema Inmunológico

Por Exceso
"Alergia"



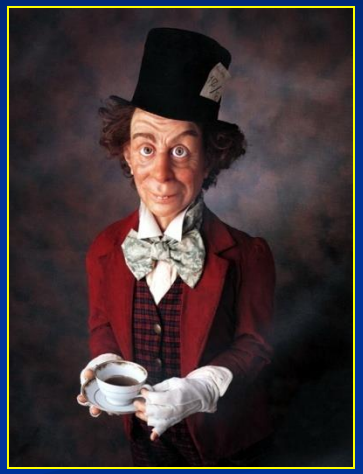
Por Defecto
"Inmunodeficiencia Primaria"



• Infecciones disfunción

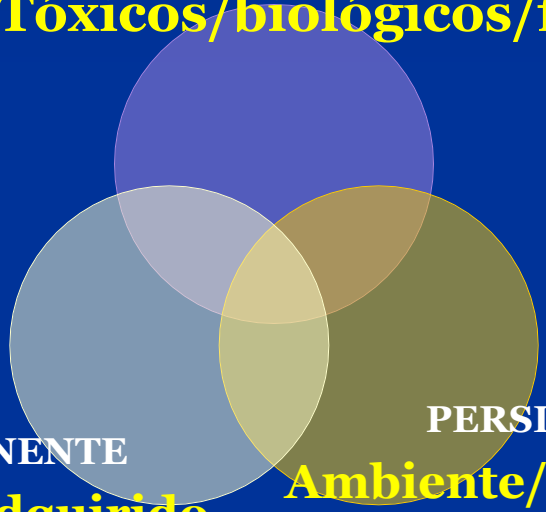
Enfermedad

"Sombrerero Loco" (Irak) trigo+mercurio



MERCURIO

Tóxicos/biológicos/físicos



PREDISPONENTE

Genético/Adquirido

PERSISTENCIA

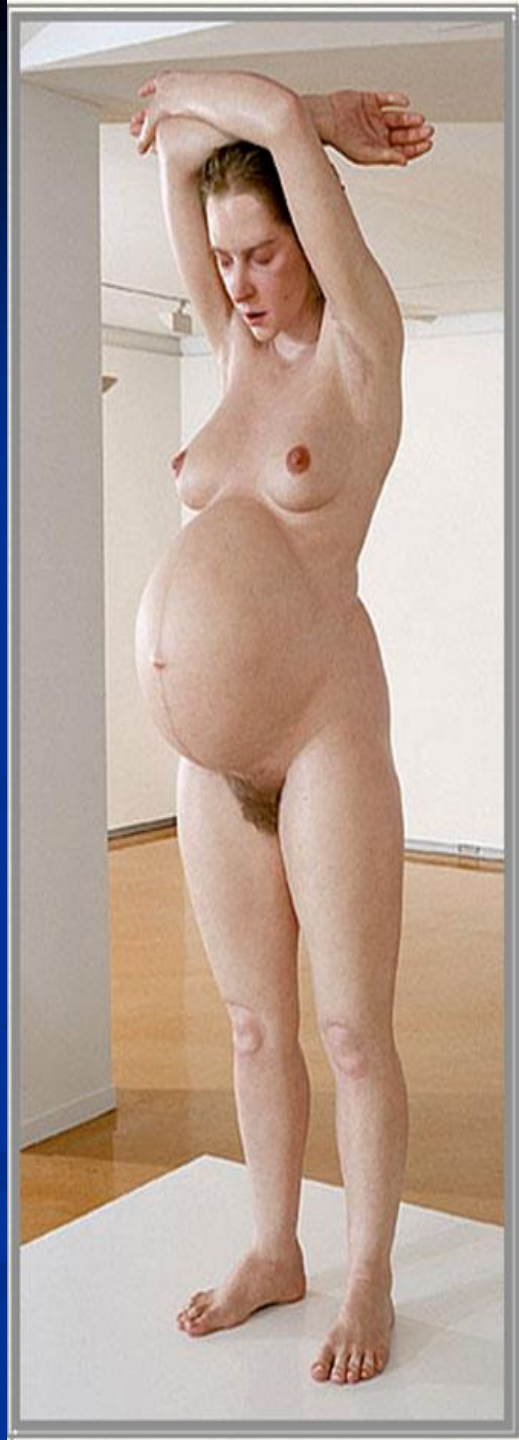
Ambiente/Estilo de Vida

El niño se convierte en victima de su ENTORNO!!!!!

Origen pre y gestacional de la enfermedad

Factores de riesgo

- Síndrome metabólico
- Enfermedad alérgica (asma)
- Sedentarismo crónico
- Depresión
- Trastornos digestivos inflamatorios
- Estrés emocional



Hipótesis de Barker: Fetal programming

1. Muchos fetos humanos tienen que adaptarse a una limitada suplencia de nutrientes. De hecho, ellos cambian permanentemente su estructura y metabolismo.

2. Esos cambios programados pueden ser el origen de un número de enfermedades mas tarde en la vida, incluyendo enfermedad coronaria y lo relacionado a accidente cerebrovascular, diabetes e hipertensión.

D. J. P. BARKER. *In utero* programming of chronic disease. Clinical Science (1998) 95, (115–128) (Printed in Great Britain)

¿Evolución o Involución?

Precipitantes

Stress Oxidativo, inflamación

"oxidación es perdida de electrones"

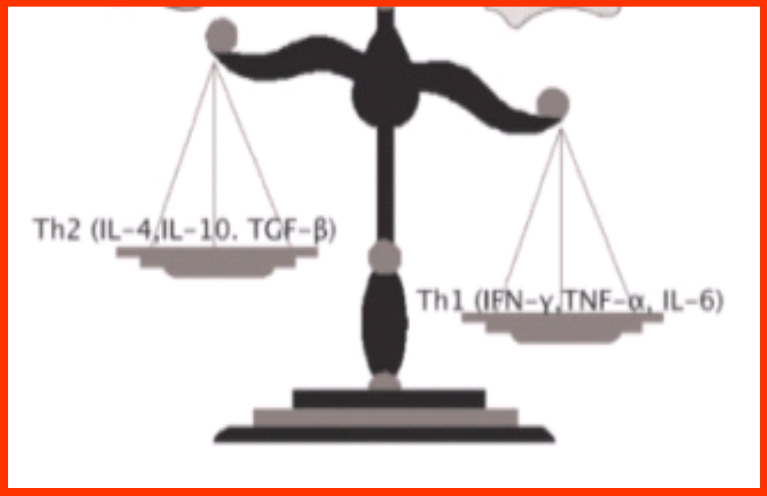
- *Quemar madera*
- *Aceite rancio*
- *Fruta marrón*

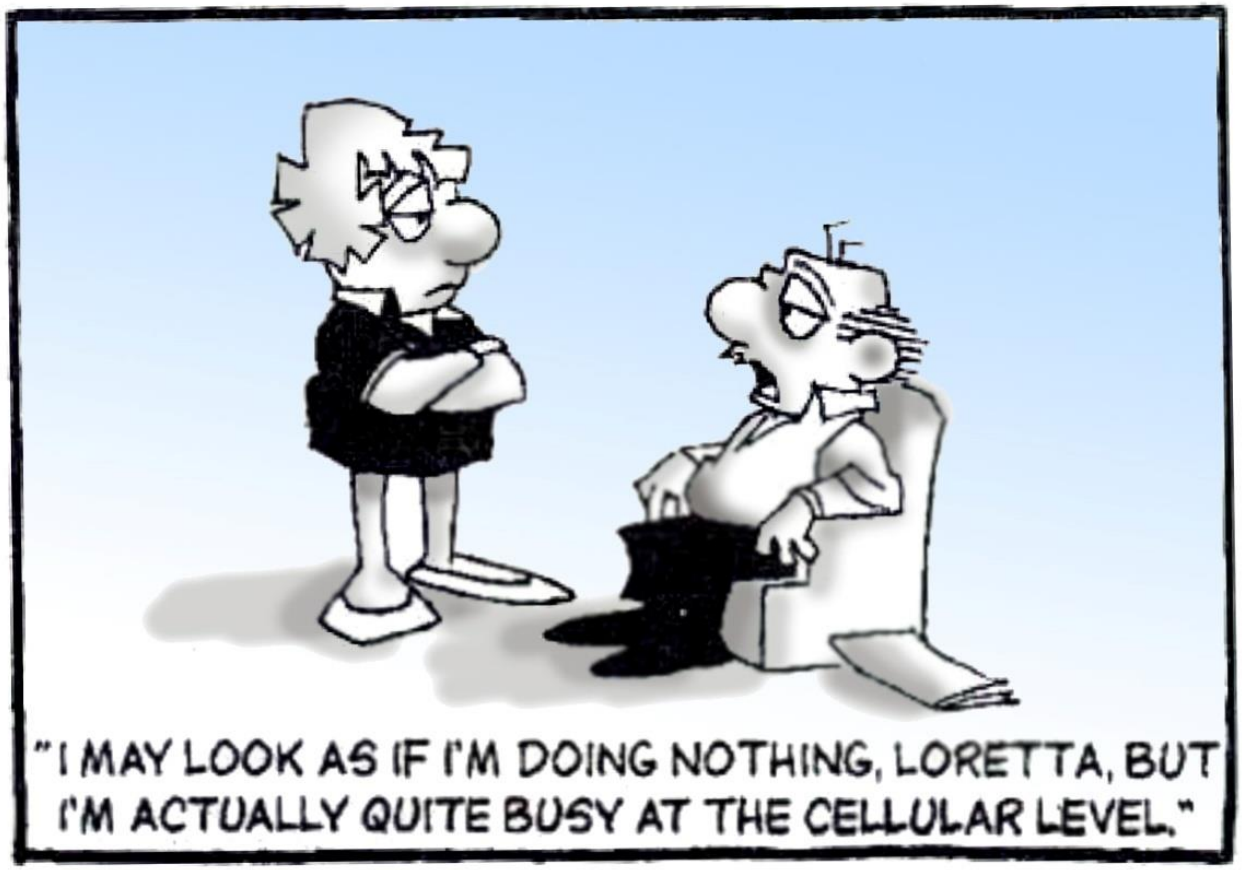
AFECTA LAS CELULAS A NIVEL MOLECULAR

Woody McGinnis 2007

Stress oxidativo es un imbalance donde los productos de oxidación sobrepasan el poder antioxidante del organismo causando defecto físico en las funciones biomoleculares

Woody McGinnis 2007

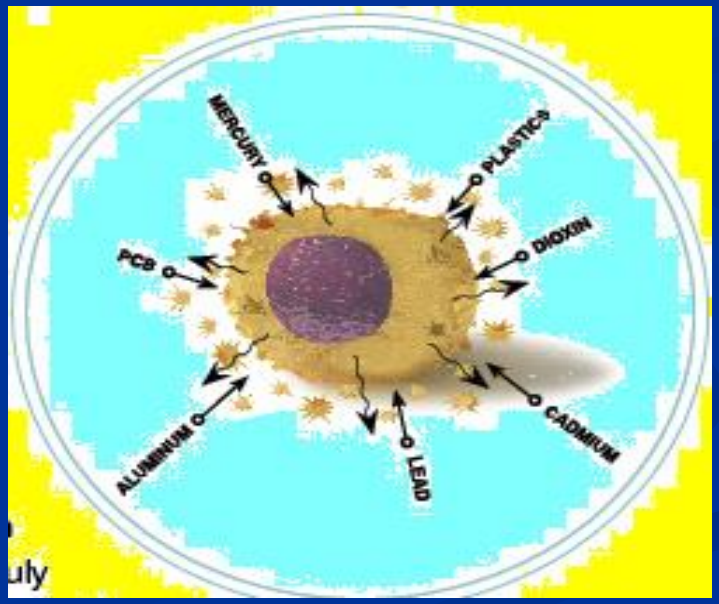



"I MAY LOOK AS IF I'M DOING NOTHING, LORETTA, BUT I'M ACTUALLY QUITE BUSY AT THE CELLULAR LEVEL."

Metales Pesados

- **Mercurio**
- **Plomo**
- **Cadmio**
- **Aluminio**
- **Arsénico**
- **Níquel**

- ✓ **Daño al DNA, RNA**
- ✓ **Mitocondrias**
- ✓ **AUTOINMUNIDAD**
- ✓ **Stress oxidativo**



The Impact of Mercury on Human Health and Environment. M.Hyman Dic.2004

Tracto Gastrointestinal

- *Estreñimiento*
- *Intestino permeable*
- *Inflamación*

!!Autismo es una condición de todo el cuerpo!!

¿Tracto Gastrointestinal?

Vol. 95, No. 9, 2000
ISSN 0002-9270/00/$20.00
PII S0002-9270(00)02041-4

Enterocolitis in Children With Developmental Disorders

A. J. Wakefield, F.R.C.S., A. Anthony, M.Sc., Ph.D., M.B.B.S., S. H. Murch, Ph.D., F.R.C.P., F.R.C.P.C.H., M. Thomson, MB.ChB., M.R.C.P., F.R.C.P.C.H., S. M. Montgomery, Ph.D., S. Davies, M.R.C.Path., J. J. O'Leary, M.D., D.Phil., M.R.C.Path., M. Berelowitz, F.R.C.Psych., and J. A. Walker-Smith, M.D., F.R.C.P., F.R.A.C.P., F.R.C.P.C.H.

University Departments of Medicine, Histopathology, Paediatric Gastroenterology, and Paediatric Psychiatry, Royal Free and University College Medical School, Royal Free Campus, London, United Kingdom, and University Department of Pathology, Coombe Women's Hospital and Trinity College, Dublin, Eire

OBJECTIVE: Intestinal pathology, *i.e.*, ileocolonic lymphoid nodular hyperplasia (LNH) and mucosal inflammation, has been described in children with developmental disorders. This study describes some of the endoscopic and pathological characteristics in a group of children with developmental disorders (affected children) that are associated with behavioral regression and bowel symptoms, and compares them with pediatric controls.

METHODS: Ileocolonoscopy and biopsy were performed on 60 affected children (median age 6 yr, range 3–16; 53 male). Developmental diagnoses were autism (50 patients), Asperger's syndrome (five), disintegrative disorder (two), attention deficit hyperactivity disorder (ADHD) (one), schizophrenia (one), and dyslexia (one). Severity of ileal LNH was graded (0–3) in both affected children and 37 developmentally normal controls (median age 11 yr, range 2–13 yr) who were investigated for possible inflammatory bowel disease (IBD). Tissue sections were reviewed by three pathologists *and scored on a standard proforma. Data were compared* with ileocolonic biopsies from 22 histologically normal children (controls) and 20 children with ulcerative colitis (UC), scored in an identical manner. Gut pathogens were sought routinely.

RESULTS: Ileal LNH was present in 54 of 58 (93%) affected children and in five of 35 (14.3%) controls ($p < 0.001$). Colonic LNH was present in 18 of 60 (30%) affected children and in two of 37 (5.4%) controls ($p < 0.01$). Histologically, reactive follicular hyperplasia was present in 46 of 52 (88.5%) ileal biopsies from affected children and in four of 14 (29%) with UC, but not in non-IBD controls ($p < 0.01$). *Active ileitis was present in four of 51 (8%) affected* children but not in controls. Chronic colitis was identified in 53 of 60 (88%) affected children compared with one of 22 (4.5%) controls and in 20 of 20 (100%) with UC. Scores of frequency and severity of inflammation were significantly greater in both affected children and those with UC, compared with controls ($p < 0.001$).

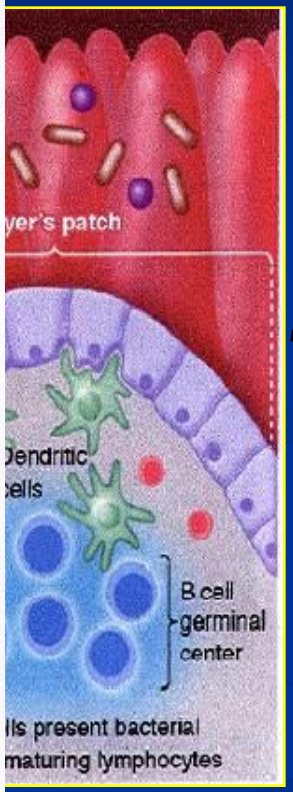
CONCLUSIONS: A new variant of inflammatory bowel disease is present in this group of children with developmental disorders. (Am J Gastroenterol 2000;95:2285–2295. © 2000 by Am. Coll. of Gastroenterology)

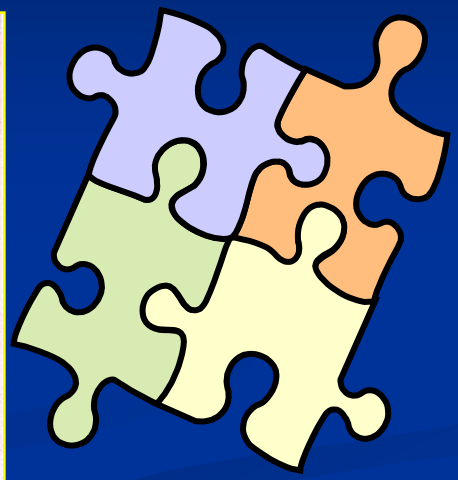
INTRODUCTION

We have recently described a characteristic pattern of intestinal inflammation in a cohort of children with developmental disorders (1). In these children, the majority of whom had autism, a period of initial normal development was followed by developmental regression and loss of acquired skills, sometimes occurring precipitously over a period of days to weeks. Long-standing intestinal symptoms, as described previously (1), were typical of this group of children. These symptoms had often started at around the same time as the behavioral changes.

Ileocolonic lymphoid nodular hyperplasia (LNH) was a consistent feature of this condition, an observation that has been reported subsequently in children with attention deficit hyperactivity disorder (ADHD) and non–IgE-mediated food allergy (2). There is an anecdotal impression that LNH is a common finding in children undergoing ileocolonoscopy, although this has not been subjected to systematic analysis in a controlled study. It cannot be assumed that LNH is a normal finding in children, as aymptomatic children are not subjected to ileocolonoscopy, and LNH may produce symptoms in its own right (3). Chronic intestinal LNH is a feature of either congenital or acquired immunodeficient states (4–10) and has been described in congenital B cell abnormalities (5, 6), and common variable immunodeficiency (7, 8). In its persistent acquired form, ileal LNH has been reported in association with infection with human immunodeficiency virus (HIV) before the development of AIDS (10).

The other consistent feature of the intestinal lesion was a mild-to-moderate colitis that lacked the specific diagnostic features of either Crohn's disease or ulcerative colitis (1). This combination of features, *i.e.*, LNH and nonspecific colitis, indicates the possibility of chronic mucosal and/or

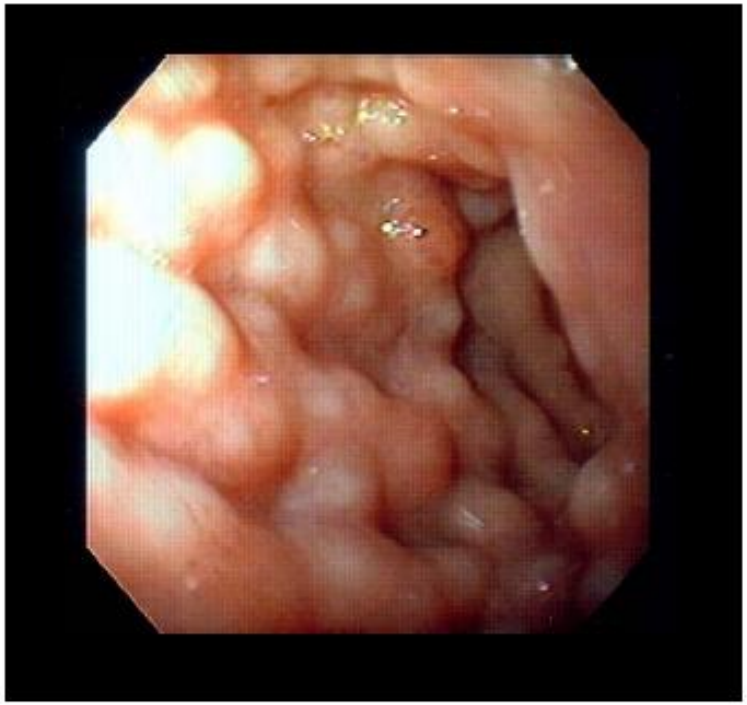


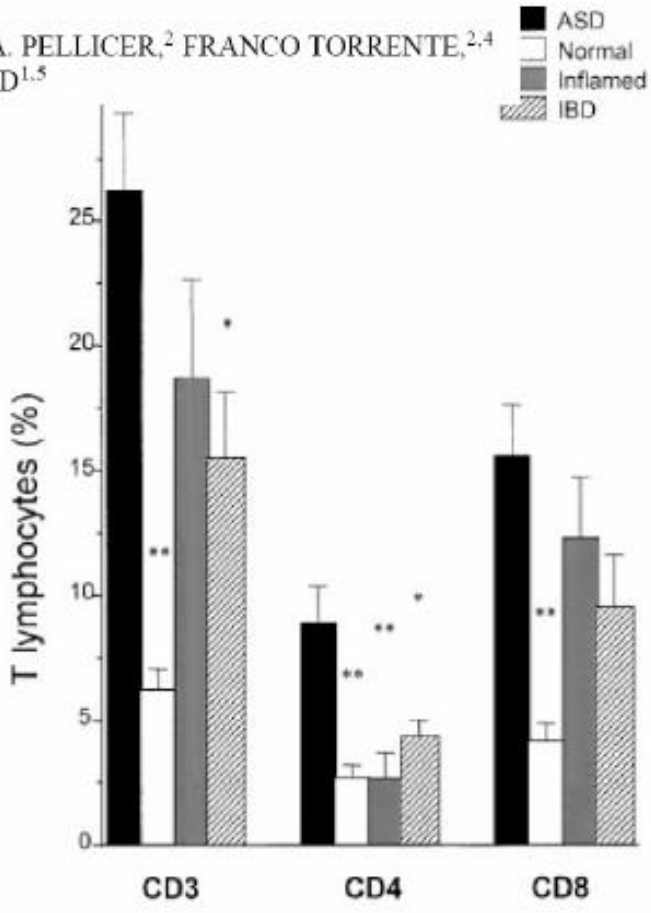


Intestinal Lymphocyte Populations in Children with Regressive Autism: Evidence for Extensive Mucosal Immunopathology

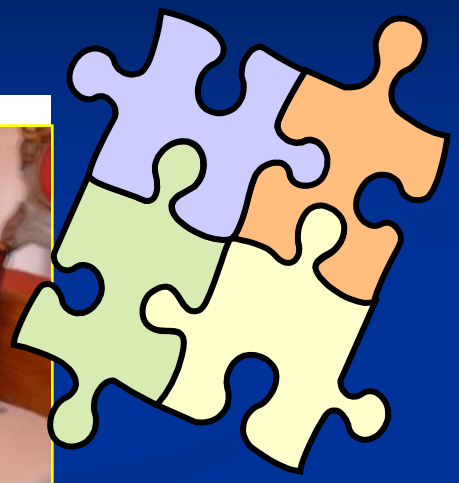
Journal of Clinical Immunology, Vol. 23, No. 6, November 2003 (© 2003)

PAUL ASHWOOD,[1,2,6] ANDREW ANTHONY,[1,3] ALICIA A. PELLICER,[2] FRANCO TORRENTE,[2,4] JOHN A. WALKER-SMITH,[2] and ANDREW J. WAKEFIELD[1,5]





¿Dolor ó conducta autista?



Digestion/Absorption

Analyte	Result	Reference Range
1. Pancreatic Elastase 1	>500	>= 201 mcg/g
2. Putrefactive SCFAs (Total*)	2.7	1.3-8.6 micromol/g

*Total values equal the sum of all measurable parts.

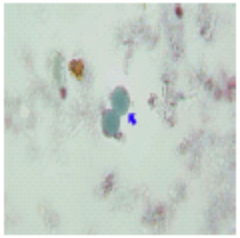
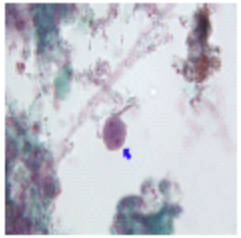
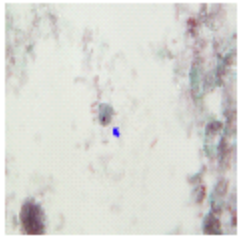
Gut Immunology

Analyte	Result	Reference Range
3. Eosinophil Protein X	>23.3	<= 7.0 mcg/g
4. Calprotectin	290	<= 50 mcg/g

Cryptosporidium	Negative
Giardia lamblia	Negative
Entamoeba histolytica/dispar	Negative

Representative photograph of organism(s)

Blastocystis hominis	Dientamoeba fragilis trophozoites	Endolimax nana trophozoites

Microbiology

Bacteriology

12. Beneficial Bacteria

Lactobacillus species		1+
Escherichia coli		1+
Bifidobacterium		*NG

13. Additional Bacteria

gamma haemolytic Streptococcus	NP	2+
Bacillus species	NP	1+
alpha haemolytic Streptococcus	NP	2+
Mucoid Escherichia coli	NP	2+
Haemolytic Escherichia coli	NP	1+

14. Mycology

Candida albicans	NP	1+

Human microflora is influenced by environmental factors and the competitive ecosystem of the organisms in the GI tract. Pathological significance should be based upon clinical symptoms and reproducibility of bacterial recovery.

*NG	NP	PP	P
*NG			
No Growth	Non-Pathogen	Potential Pathogen	Pathogen

Trastornos metabólicos

- **Sobrecarga de metales pesados-Stress Oxidativo**

-mercurio, arsénico, plomo

-Depleción de antioxidantes, Glutation y Metalotioneina

-Deficiencia de Zinc, Magnesio

- **Debil Detoxificación**

-defectos de la metilación y remetilación

-defectos de la sulfación

-deficiencia de cisteina

-deficiencia del glutation (GSH)

Oxidative Stress

Reducir stress

Methylation and Transsulfation

suplementar

Immunological

Tratar infecciones

Heavy Metals

Remover tóxicos

Jeff Bradstreet 2007

Alimento de uno es veneno de otro

Péptido derivados de alimentos:
GLUTEN Y CASEINA 1980

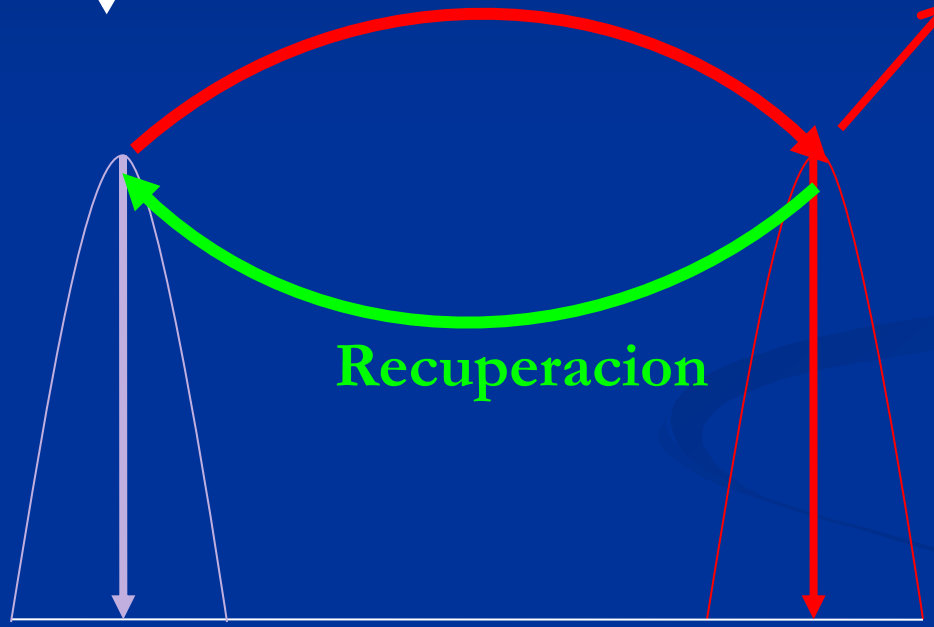
Moléculas que actúan como opioides (morfina , heroína o narcóticos), SE UNEN A RECEPTORES gluteo y cáseo morfina

neurotransmisores / inmunomoduladores

Exposicion toxica, inflamacion,
infeccion , envejecimiento

Redox
celular
ideal

Perdida de funcion
celular normal
reduccion
de la metilacion



$\frac{GSH}{GSSG} = 30$

$\frac{GSH}{GSSG} = 10$

Exposicion toxica, inflamacion, infeccion , envejecimiento

Redox celular ideal

Perdida de funcion celular normal reduccion de la metilacion

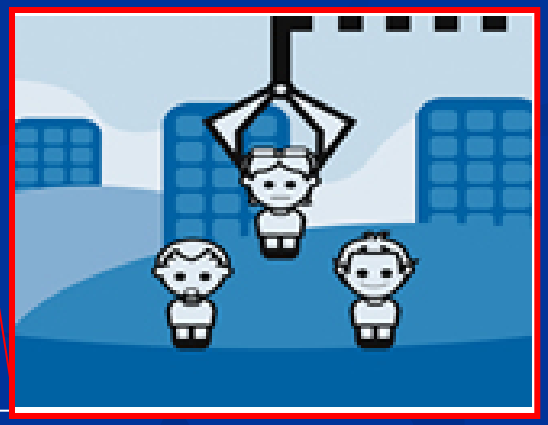
Estress Oxidativo

GSH Utilization > Supply

GSH Utilization < Supply

Recovery

Autismo?



$\frac{GSH}{GSSG} = 30$

Ambiente menos oxidante

$\frac{GSH}{GSSG} = 10$

Ambiente mas oxidante

Vulnerabilidad a stress oxidativo??????

Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism.

James SJ, Melnyk S, Jernigan S, Cleves MA, Halsted CH, Wong DH, Cutler P, Bock K, Boris M, Bradstreet JJ, Baker SM, Gaylor DW (Goldblatt A)

Am J Med Genet B Neuropsychiatr Genet. 2006 Aug 17

Plasma levels of metabolites in methionine transmethylation and transsulfuration pathways were measured in 80 autistic and 73 control children. In addition, common polymorphic variants known to modulate these metabolic pathways were evaluated in 360 autistic children and 205 controls. The metabolic results indicated that plasma methionine and the ratio of S-adenosylmethionine (SAM) to S-adenosylhomocysteine (SAH), an indicator of methylation capacity, were significantly decreased in the autistic children relative to age-matched controls. In addition, plasma levels of cysteine, glutathione, and the ratio of reduced to oxidized glutathione, an indication of antioxidant capacity and redox homeostasis, were significantly decreased. Differences in allele frequency and/or significant gene-gene interactions were found for relevant genes encoding the reduced folate carrier (RFC 80G > A), transcobalamin II (TCN2 776G > C), catechol-O-methyltransferase (COMT 472G > A), methylenetetrahydrofolate reductase (MTHFR 677C > T and 1298A > C), and glutathione-S-transferase (GST M1). **We propose that an increased vulnerability to oxidative stress (endogenous or environmental) may contribute to the development and clinical manifestations of autism.**

Trastornos metabólicos

- **Disfunción gastrointestinal**

-disbiosis (levaduras, virus, bacterias)

-malabsorción

-mala digestión (deficiencia enzimático, sensibilidad IgG alimentos, péptidos urinarios)

-enterocolitis autística –hiperplasia linfonodular

- **Disregulación del sistema Inmune**

-citoquinas proinflamatorias

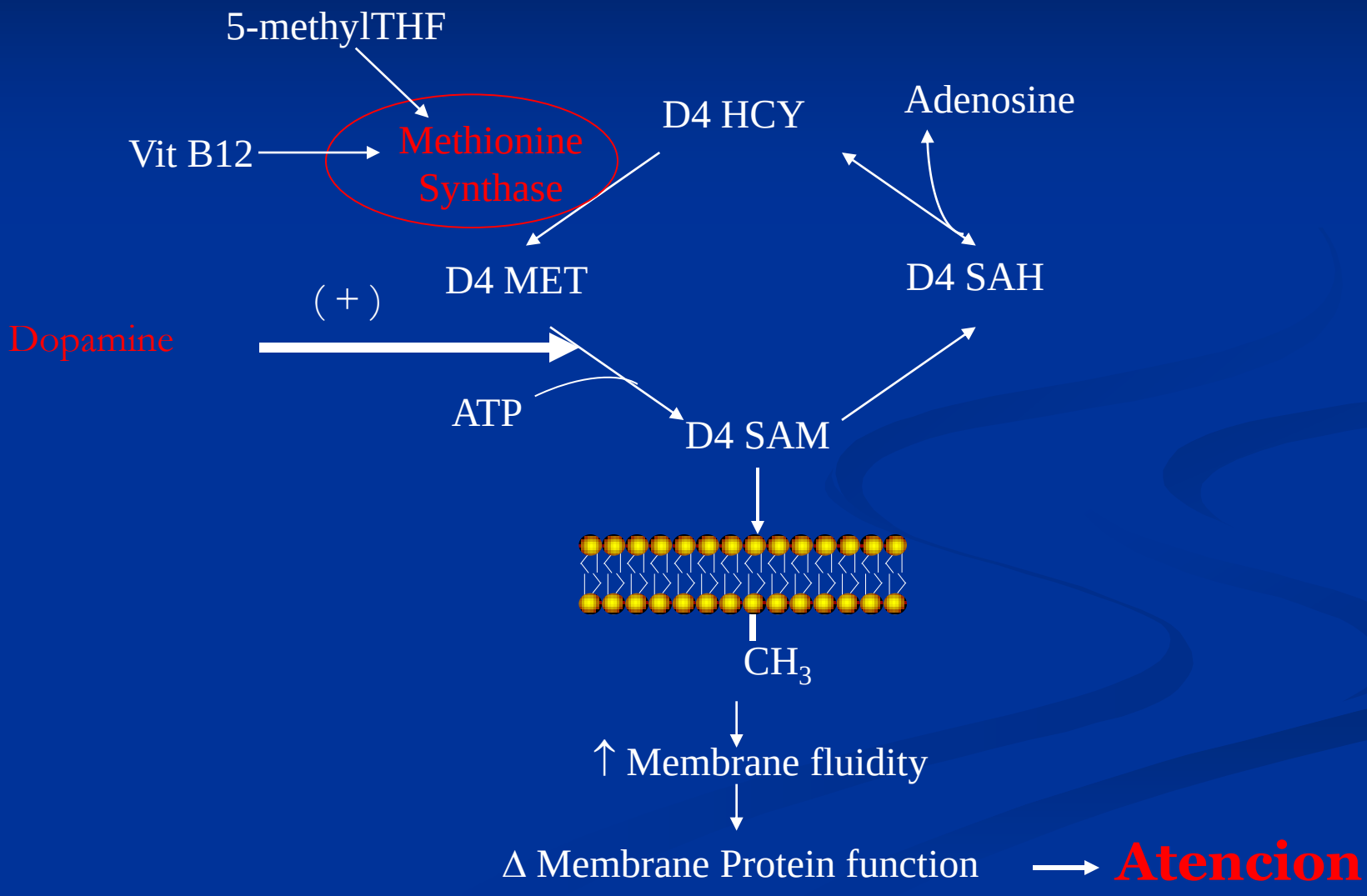
-activación microglia

-Th1-Th2 no balanceada

-disminución de actividad NK

-aumento de marcadores de auto inmunidad

El receptor D4 en el ciclo de la metilacion de Fosfolipidos



Fundamento del Enfoque Biomedico. Aprobado por ARI

- Mejoras en la Dieta
- Alergias a Alimentos
- Dieta sin gluten, caseina o productos
- Suplementos vitamínicos y minerales
- Altas dosis de Vitamina B6 y Magnesio
- Acidos grasos escenciales
- Aminoácidos
- Tratamientos digestivos
- Suplementos de la Tiroides
- Sulfatación
- Glutiationes
- Detoxificación
- Tratamientos anti-virales
- Regulación del Sistema inmunológico

Autism Research Institute
Since 1967
Autism Is Treatable!

DAN!
Defeat Autism Now!

Remover irritantes		Apoyar capacidad de curacion
Reducir stress	⟺	Estimular plasticidad cerebral
suplementar	⟺	soporte para detoxificacion
Tratar infecciones	⟺	soporte Inmune
Remover toxicos	⟺	capacidad de regeneracion

ALGORITMO

NIVEL #1 ↓

CONTROL DE NIÑO SANO

Evaluar ☹

- **NO BALBUCEO, NO SEÑALAR O GESTOS A LOS 12 MESES, NO MIRA**
- **NO HAY PALABRAS 16 MESES,**
- **NO 2 PALABRAS ESPONTANEAS,**
- **NO FRASES 24 MESES,**
- **CUALQUIER PERDIDA DEL LENGUAJE O APRENDIZAJE SOCIAL!!!! ☹**

↓

Raspado Laboratorio ← → **Aprobado**

↓

Referir a nivel 2

↘

RE-EVALUAR

ALGORITMO

NIVEL #2

Evaluar ☹ Diagnóstico formal:

- **CLINICO: HISTORIA**
- **NEUROLOGO**
- **GASTROENTEROLOGO**
- **INMUNOLOGO**
- **LABORATORIO**

REFERIDO A INTERVENCION

☺

Neurology, Filipek et al, 2000,55:468:479

Evaluación

Laboratorio#1

Laboratorio General:

- Perfil General
- Perfil Anemia
- Perfil Tiroideo
- Perfil Inmunológico
- Metab☻lico: aminoacidos
- Perfil Tóxico: metales cabello,orina

REFERIDO A INTERVENCION

☺

Protocolo DAN 2006, Washington Mayo

Evaluación

Laboratorio#2

Laboratorio Especial

- Analisis de heces USA
- Laboratorio Estress oxidativo
- Acidos organicos
- Genetico

REFERIDO A INTERVENCION

Protocolo DAN 2006, Washington Mayo

URINE TOXIC METALS

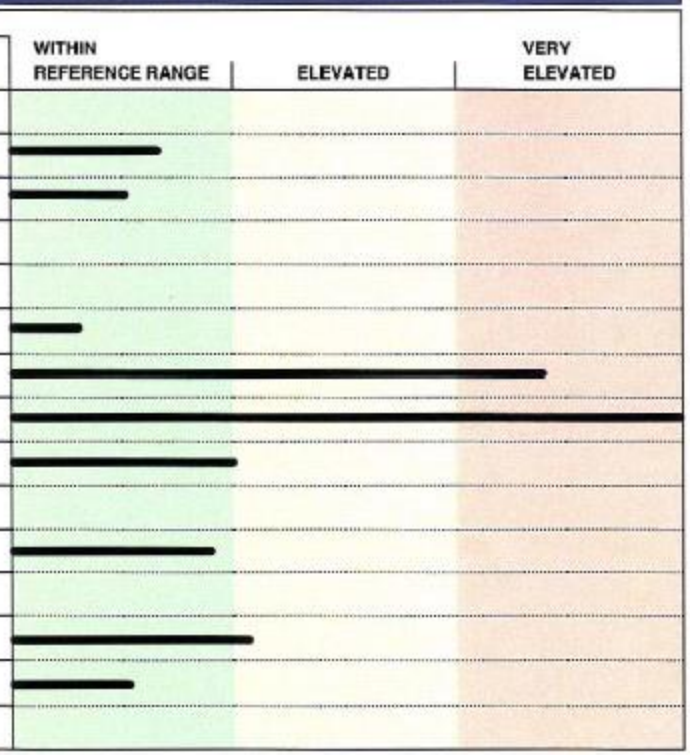
DOCTOR'S DATA INC

LAB#: U051103-0454-1
PATIENT:
SEX: Male
AGE: 6

CLIENT#: 24503
DOCTOR: James Jeff Bradstreet, MD
International Autism Research
1688 W Hibiscus Blvd
Melbourne, FL 32901

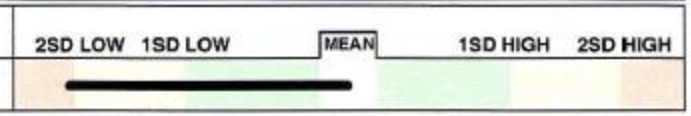
POTENTIALLY TOXIC METALS

METALS	RESULT µg/g CREAT	REFERENCE RANGE
Aluminum	< dl	< 60
Antimony	1	< 1.5
Arsenic	67	< 130
Beryllium	< dl	< 0.6
Bismuth	< dl	< 20
Cadmium	0.6	< 2
Lead	28	< 5
Mercury	40	< 5
Nickel	16	< 15
Platinum	< dl	< 1
Thallium	1	< 1.1
Thorium	< dl	< 0.5
Tin	20	< 15
Tungsten	0.8	< 1.5
Uranium	< dl	< 0.2



CREATININE

	RESULT mg/dL	REFERENCE RANGE
Creatinine	21	25- 180



SPECIMEN DATA

Biomarcadores

- ***Stress oxidativo*:>Orina:** 8 –OHG, Isoprostane>**Sangre**: Transferrina, Ceruloplasmina,Amonio, Lactato, Glutation Reducido, GSSG

- ***Metilación y transulfación***:>**Plasma:** Cysteina y Metionina en Ayunas

- ***Inmunológico*:>orina:** Neopterin y Biopterin>**sangre**: Anticuerpos Anti-endotelial ASTO, antiDNASA B, IgG sub, IgA,IgM,IgG,IgE, contaje

- ***Metales pesados*:>sangre**: Eritrocitos minerales y tóxicos> Metalotioneina en linfocitos pre y post inducción,**>orina** Porfirinas fraccionadas si elevadas post qelación (6 horas)

- ***Perfil metabólico*:**>sangre: electrolitos, función hepática y renal, química amonio, anión gap

- ***Util*:** ácidos orgánicos urinarios, oxalatos urinarios

Porfirinas urinarias: Mercurio

J.S. Woods et al. / Toxicology and Applied Pharmacology 206 (2005) 113–120

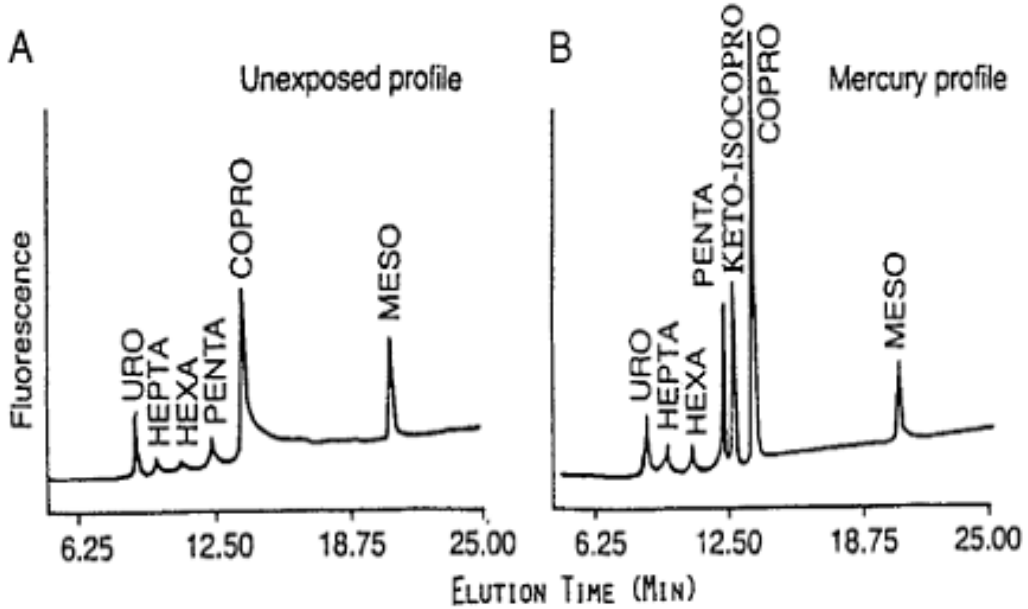


Fig. 1. HPLC urinary porphyrin profiles from: (A) unexposed and (B) mercury-exposed subjects. Abscissa is elution time in minutes. Ordinate is relative porphyrin concentration in fluorescence units. Porphyrins were measured as described in Methods. URO = uroporphyrin, HEPTA = hepta-carboxyporphyrin, HEXA = hexa-carboxylporphyrin, PENTA = pentacarboxylporphyrin, COPRO = coproporphyrin, KETO-ISOCOPRO = ketoisocoproporphyrin, MESO = mesoporphyrin (an internal standard).

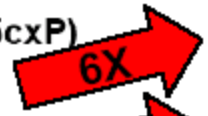
THE ATYPICAL KETO-ISOCOCPROPHYRIN = PRECO IN NATAF STUDY

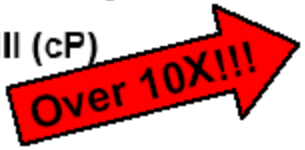
Dr.Nataf.Francia DAN Meeting , Virginia , USA. Mayo 2007

Urinary porphyrins

HPLC-UV+Fluorescence

		(nmol)		reference		Interpretation
				nanomoles/gr Cr urinary		
					%	
Uroporphyrins I &III (UP)		**15**	nmol	7-14	*1*	Slighltly increased rate
Heptacarboxy porphyrin (7cxP)		**5,1**	nmol	1,5-3,5	*0,5*	Slighltly increased rate
Hexacarboxy porphyrin (6cxP)		**0,6**	nmol	0,4-0,8	*0,0*	Average Rate
Pre 5-Carboxy-P		**1,1**	nmol			
Pentacarboxy porphyrin (5cxP)		**12,8**	nmol	1,0-2,9	*1,3*	Increased rate
Precoporphyrin (prCP)		**32,6**	nmol	2-5		Increased rate
Coproporphyrins I & III (cP)		**858**	nmol	50-80	*95*	Increased rate
prCP/UP	PrecoP/Uro ratio	**2,05**		0,3-0,6		
UP / CP	uro/copro ratio	**0,01**		0,14-0,1		





Porphyrinuria in Childhood Autistic Disorder: Implications for Environmental Toxicity

Robert Nataf a, Corinne Skorupkab, Lorene Ametb, Alain Lama, Anthea Springbettc, Richard Lathed
Laboratoire Philippe Auguste, Paris, France

Toxicol Appl Pharmacol. 2006 Jun 15; [Epub ahead of print]

The atypical molecule precoproporphyrin, a specific indicator of heavy metal toxicity, was also elevated in autistic disorder, N=106 ($p<0.001$) but not significantly in Asperger's N=11. A subgroup with autistic disorder was treated with oral dimercaptosuccinic acid (DMSA) N= 11, with a view to heavy metal removal. There was a significant ($p=0.002$) drop in urinary porphyrin excretion following DMSA. These data implicate environmental heavy metal toxicity in childhood autistic disorder.

Detoxificación

- Historia y examen físico
- Terapias de limpieza
  - -limpiar el ambiente
  - -limpiar la dieta
  - -limpiar el intestino
- Terapias de nutrientes
- Laboratorios
- Tratar inbalances bioquímicos y nutricionales
- Detoxificación hepática
- Detox de metales pesados

Heavy metals like mercury and lead must be removed while protecting the required nutrient minerals: Zinc, Selenium, etc

Intensidad de Sintomas = Intensidad de tratamiento

Mas agresivo mas efectos adversos!

Anju I.Usman,MD Noviembre 2005

No se a dectectado Autismo en la población Amish, Dr. Frank Noonan, medico familiar del condado de Lancaster Pa.

The Age of Autism. Dan Olmsted July 2006

Dietas

- Libre de Caseina , Gluten (CF-GF)
- Dieta específica de carbohidratos (SCD)
- Dieta ecológica (BED)
- D
- D
- Dieta baja en Excitocinas
- Dieta de Rotación-Dieta de Eliminación
- Dieta baja Cobre
- Dieta baja en Oxalatos

Aditivos, MSG, benzoatos, sulfitos, edulcorantes artificiales, embutidos , enlatados, envasados

Se ha demostrado que la dieta rica en antioxidantes puede influir positivamente en la disminución de alergias y de asma.

Romieu I, Trenga C. Diet and obstructive lung diseases. Epidemiol Rev 2001;23:268–87.

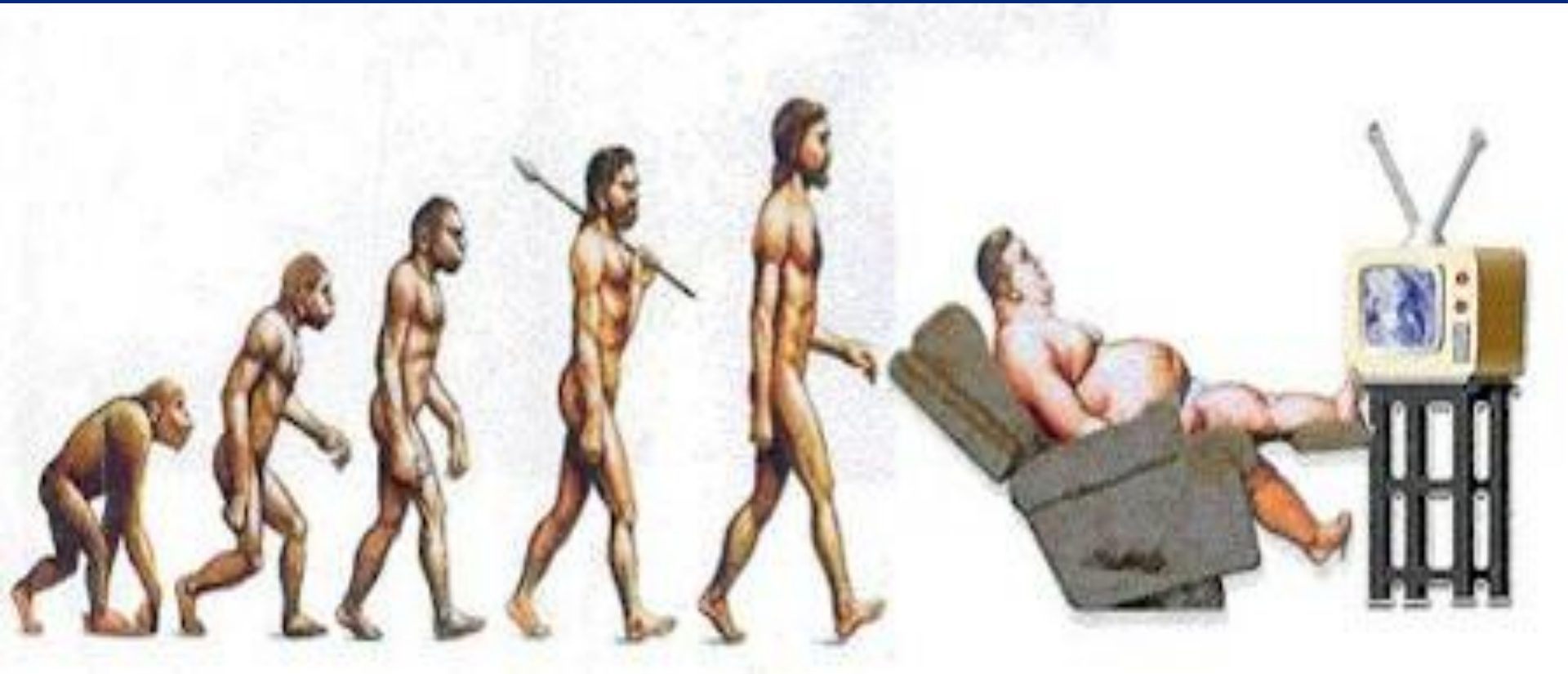
Terapias Nutrientes básicos

- Antioxidantes (Vit A,C,E,Se)
- Vitamina B6-P5P,B complex
- Minerales (Zinc, Magnesio,Molibdeno…)
- Omega 3 EFA (Aceite de Higado de Bacalao)
- Methyl B12 inyectado
- Baños de Sal de Epson
- Probióticos

Detoxificación hepática

- Metilación (agregar un CH_3)
- Sulfación (agregar un SO_4)
- Conjugación de aminoacidos
  - Glicina , DMG,TMG
  - Taurina (con Mg)
- Glutation
- Acetilación (n-acetyl cisteina, glucosamina)
- Glucuronidación (calcio d-glucarate)

¿Evolución o Involución?



☺☺☺ Detoxificación!!!!!

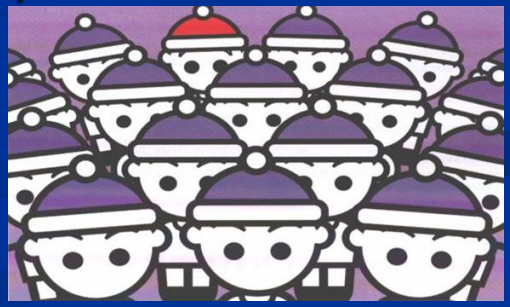
- **¿Quelación? ("Chelation")**

"Chele", en giego significa la tenaza de la langosta o cangrejo.

- **Quien "agarra o atrapa" los metales?** ***ALA, cisteina, N Acetyl Cysteina, EDTA, DMSA, DMPS, TTFD***

- **Vias para Quelación:** ***oral, endovenoso, trans-térmico, supositorios .***

- ***Referido por los padres como con un* 65%a 72% eficacia!!!!!! Mejoraron 34:1**



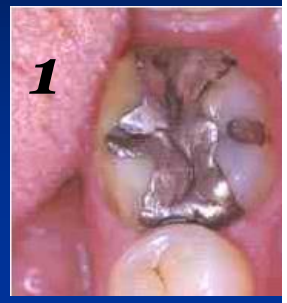
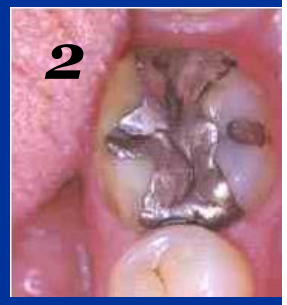
Meeting report, Autism Conference reports adances in early diagnosis,role of immune System and more **mayo 2005**

Quelacion

El mercurio desactiva la cadena de la metilación!!!!!!!!!!! (daña los thioles) cont.

- thiol="mercaptan"(moleculas <con átomo de sulfuro)
- mercaptan="mer(cury)-cap(ture)"= moléculas que capturan mercurio! 1820
- moléculas con sulfuros (quelantes) 2005
- Quelantes que rescatan nuestra bioquímica Envenenada por metales pesados!!!!!

Meeting report, Autism Conference reports adances in early diagnosis,role of immune System and more **mayo 2005**




DOCTOR'S DATA Inc.

LAB#: H070205-0343-1
PATIENT: Lernio Caballero Perez
SEX: Male
AGE: 3

CLIENT#: 28641
DOCTOR: Lorena Benarroch, MD
Hospital Clinicas Caracas
Apartado 68767 Altamira 1062
Caracas, 1062 VENEZUELA

POTENTIALLY TOXIC ELEMENTS

TOXIC ELEMENTS	RESULT µg/g	REFERENCE RANGE
Aluminum	38	< 8.0
Antimony	0.18	< 0.066
Arsenic	0.12	< 0.080
Beryllium	< 0.01	< 0.020
Bismuth	0.52	< 0.13
Cadmium	0.22	< 0.15
Lead	11	< 1.0
Mercury	0.19	< 0.40
Platinum	< 0.003	< 0.005
Thallium	0.001	< 0.010
Thorium	< 0.001	< 0.005
Uranium	0.013	< 0.060
Nickel	0.46	< 0.40
Silver	2.3	< 0.20
Tin	1.2	< 0.30
Titanium	0.64	< 1.0
Total Toxic Representation		

PERCENTILE: 68th, 86th

ESSENTIAL AND OTHER ELEMENTS

ELEMENTS	RESULT µg/g	REFERENCE RANGE
Calcium	317	125 - 370
Magnesium	26	12 - 30
Sodium	380	12 - 90
Potassium	600	12 - 40
Copper	14	8.0 - 16
Zinc	57	100 - 190
Manganese	0.45	0.20 - 0.55
Chromium	0.73	0.26 - 0.50
Vanadium	0.15	0.030 - 0.10
Molybdenum	0.10	0.050 - 0.13
Boron	4.3	0.60 - 4.0
Iodine	1.2	0.25 - 1.3
Lithium	0.008	0.007 - 0.023
Phosphorus	215	160 - 250
Selenium	1.1	0.95 - 1.7
Strontium	0.75	0.16 - 1.0
Sulfur	43700	45500 - 53000
Barium	1.3	0.16 - 0.80
Cobalt	0.019	0.013 - 0.035
Iron	20	8.0 - 19
Germanium	0.034	0.045 - 0.065
Rubidium	0.65	0.016 - 0.18
Zirconium	0.20	0.040 - 1.0

PERCENTILE: 2.5th, 16th, 50th, 84th, 97.5th

SPECIMEN DATA

COMMENTS:

Date Collected: 1/16/2007
Date Received: 2/5/2007
Date Completed: 2/9/2007

Methodology: ICP-MS

Sample Size: 0.2 g
Sample Type: Head
Hair Color: Black
Treatment:
Shampoo: Jj

W6.00

RATIOS

ELEMENTS	RATIOS	EXPECTED RANGE
Ca/Mg	12.2	4 - 30
Ca/P	1.47	0.8 - 8
Na/K	0.633	0.5 - 10
Zn/Cu	4.07	4 - 20
Zn/Cd	259	> 800

¨!No tratar a la enfermedad sino al enfermo!¨

- **¿Asumimos que todos tienen el mismo problema?**
- **Diferencias inter-individuales.**
- **La razón para la suceptibilidad individual amerita atención.**
- **Enfermedad crónica compleja y multifactorial.**

Meeting report, Autism Conference reports adances in early diagnosis,role of immune System and more **mayo 2005**

Camara Hiperbarica

Hyperbaric oxygen therapy may improve symptoms in autistic children

Med Hypotheses. 2006;67(2):216-28. Epub 2006 Mar 22.

Daniel A. Rossignol [a,b,*], **Lanier W. Rossignol**

[a] *Blue Ridge Medical Center, 4038 Thomas Nelson Highway, Arrington, VA 22922, USA*
[b] *University of Virginia, P.O. Box 800729, Charlottesville, VA, USA*

Neuropeptidos intrigantes con poco riesgo usados adecuadamente!!!!!!!!!!!!!!!

EDITORIAL

Oxitocina/ Secretina

Secretin's role in the cerebellum: A larger biological context and implications for developmental disorders

MARTHA G. WELCH[1], ROBERT J. LUDWIG[1], MARK OPLER[3] & DAVID A. RUGGIERO[1,2]

Departments of [1]Psychiatry and [2]Anatomy, College of Physicians & Surgeons, Columbia University, and [3]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, USA

"It is more reasonable to suspect that long-range effects on stress adaptation response patterns will require continuous or serial administration of peptide combinations *(oxytocin and secretin)* over many days, in a way that more closely replicates maternal nurture mechanisms that naturally stimulate the synthesis and release of stress regulatory peptides".

Spironolactona

Medical Hypotheses (2006) x, xxx–xxx

ELSEVIER

medical hypotheses

http://intl.elsevierhealth.com/journals/mehy

Spironolactone might be a desirable immunologic and hormonal intervention in autism spectrum disorders

James Jeffrey Bradstreet [a], Scott Smith [a], Doreen Granpeesheh [b], Jane M. El-Dahr [c], Daniel Rossignol [d,*]

Summary Multiple studies now demonstrate that autism is medically characterized, in part, by immune system dysregulation, including evidence of neuroglial activation and gastrointestinal inflammation. This neuroglial process has further been characterized as neuroinflammation. In addition, a subset of autistic children exhibit higher than average levels of androgens. Spironolactone is an aldosterone antagonist and potassium-sparing diuretic with a desirable safety profile. It possesses potent anti-inflammatory and immune modifying properties that might make it an excellent medical intervention for autism spectrum disorders. Furthermore, spironolactone possesses potent anti-androgen properties that might further enhance its appeal in autism, particularly in a definable subset of hyperandrogenic autistic children. One case report is briefly reviewed demonstrating objective clinical improvements in an autistic child after spironolactone administration. Additional research in controlled trials is now needed to further define the risks and benefits of spironolactone use in children with autism.

...las piezas van cuadrando

Hay Solución?

Sontag LW. Significance of fetal environmental differences. *Am J Obstet Gynecol.* 1941;42:996–1003. en Hobel Calvin J. Stress and Preterm Birth. Clinical Obstetrics And Gynecology. December 2004; 47(4):856-880.

Autismo es un problema de DE SALUD PUBLICA!!!!!!!!!!

No un problema psicológico

La mayoría de los pacientes tienen

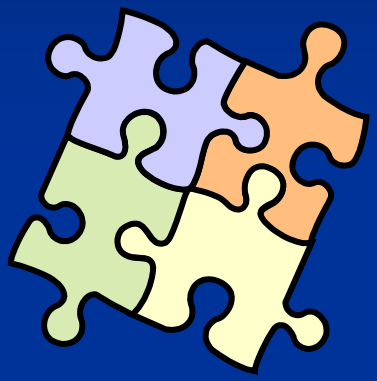
TOXICIDAD ☹☹

inducida por el medio-ambiente

Por lo tanto El Autismo es ☺ ☺ ☺

PREVENIBLE, REVERSIBLE Y TRATABLE

Autismo es incurable: evidencia es pobre



Tratamiento y recuperación son posibles:

evidencia es real!!!!!!

Gracias