

THE EPIDEMIC IN BRAIN–IMMUNO–GUT DISORDERS: WHY?

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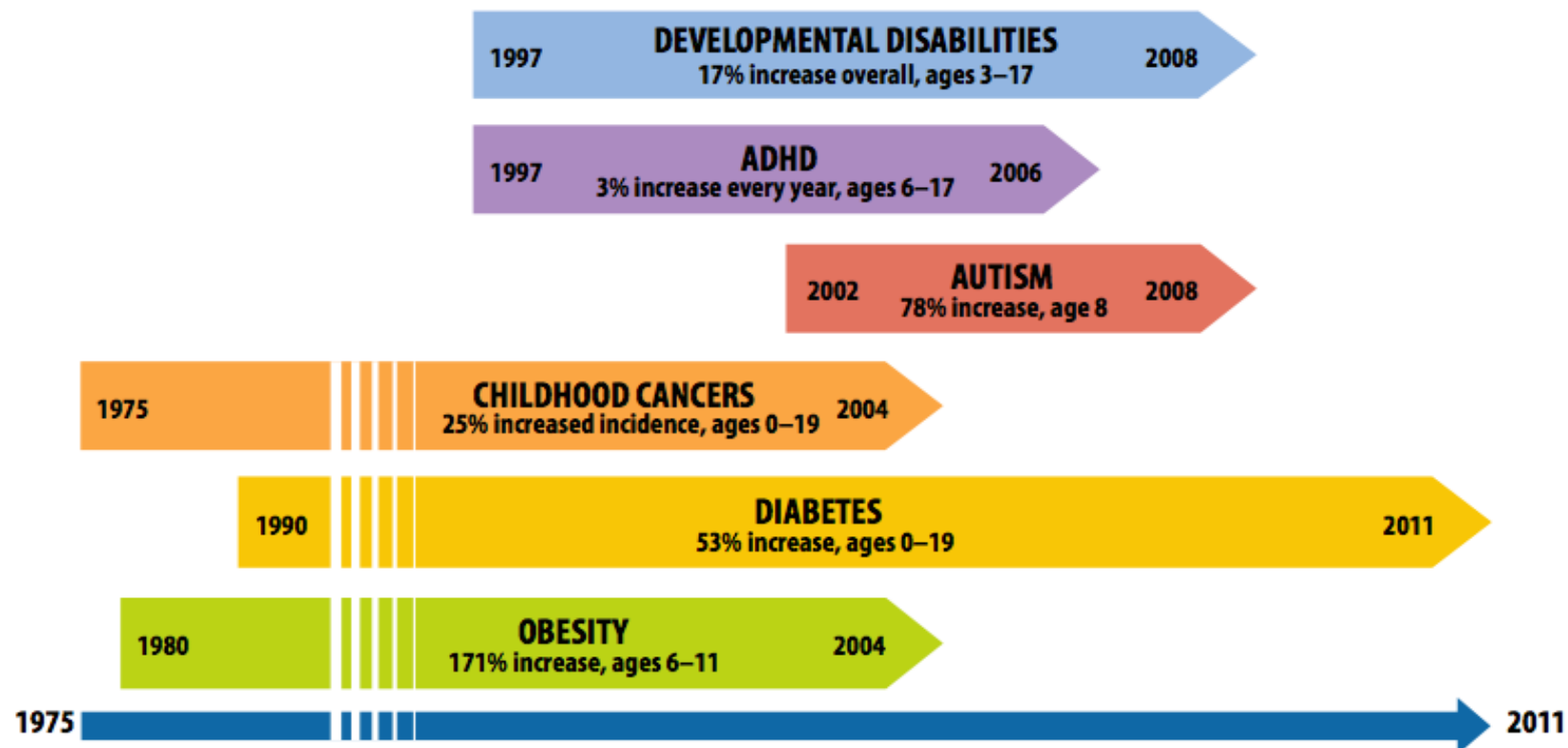
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Childhood conditions on the rise

Figure 1: Children's Health Harms on the Rise, 1975–2011*



Statistics show steady increases in many childhood diseases and disorders over the past 30 years. Those highlighted here are just some of the health harms on the rise.
Sources: see endnotes 4, 13, 24, 52 and 94.

The A's

- ▶ Asthma, allergies (atopy), ADHD, autism all dramatically increased over past 20 years
- ▶ Allergies up to 7x, affecting up to 50% children
- ▶ Asthma point prevalence peak 36% (2002):
Australia 3rd highest prevalence rate in the world
- ▶ Asthma incidence reduced but eczema increased:
now affects 1 / 3 people (Aus) at some stage in life,
(2010) 50% by age 1 year, 30% between 1 and 5
years, total >25% children
- ▶ nearly 30% children with food allergies

All share an underlying immune system shift

- ▶ Th2 shift
- ▶ Immune system skewed to antibody production
- ▶ Corresponding reduction in Th1 immunity

US disease trends

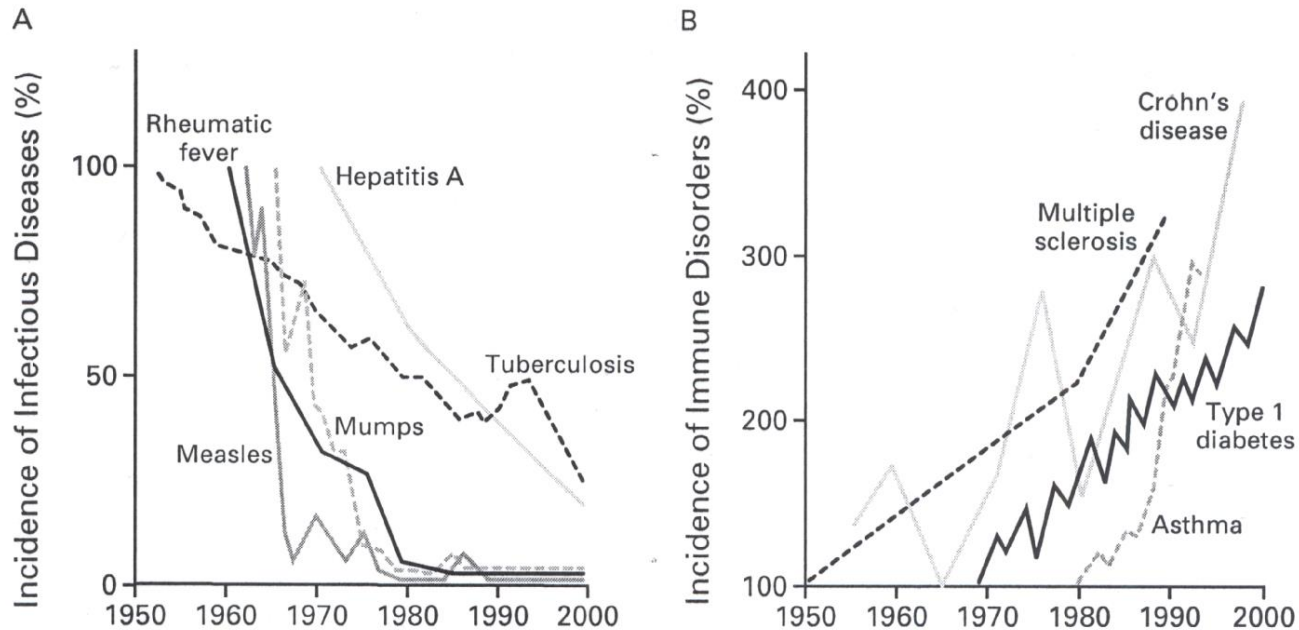


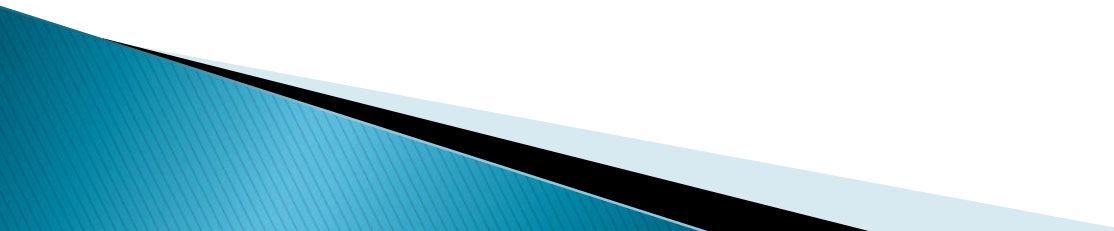
Figure 1. Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

In Panel A, data concerning infectious diseases are derived from reports of the Centers for Disease Control and Prevention, except for the data on hepatitis A, which are derived from Joussemet et al.¹² In Panel B, data on immune disorders are derived from Swarbrick et al.,¹⁰ Dubois et al.,¹³ Tuomilehto et al.,¹⁴ and Pugliatti et al.¹⁵

INFECTIONS

- ▶ Concomitant rise in various infections which were not vaccinated against:
- ▶ Otitis media (2000): 91% children by age 2 years
- ▶ Sinusitis: now common
- ▶ Gastrointestinal infections:
- ▶ Respiratory tract infections: hospital admissions increase 3.7% per year, total 40%

Mental Health

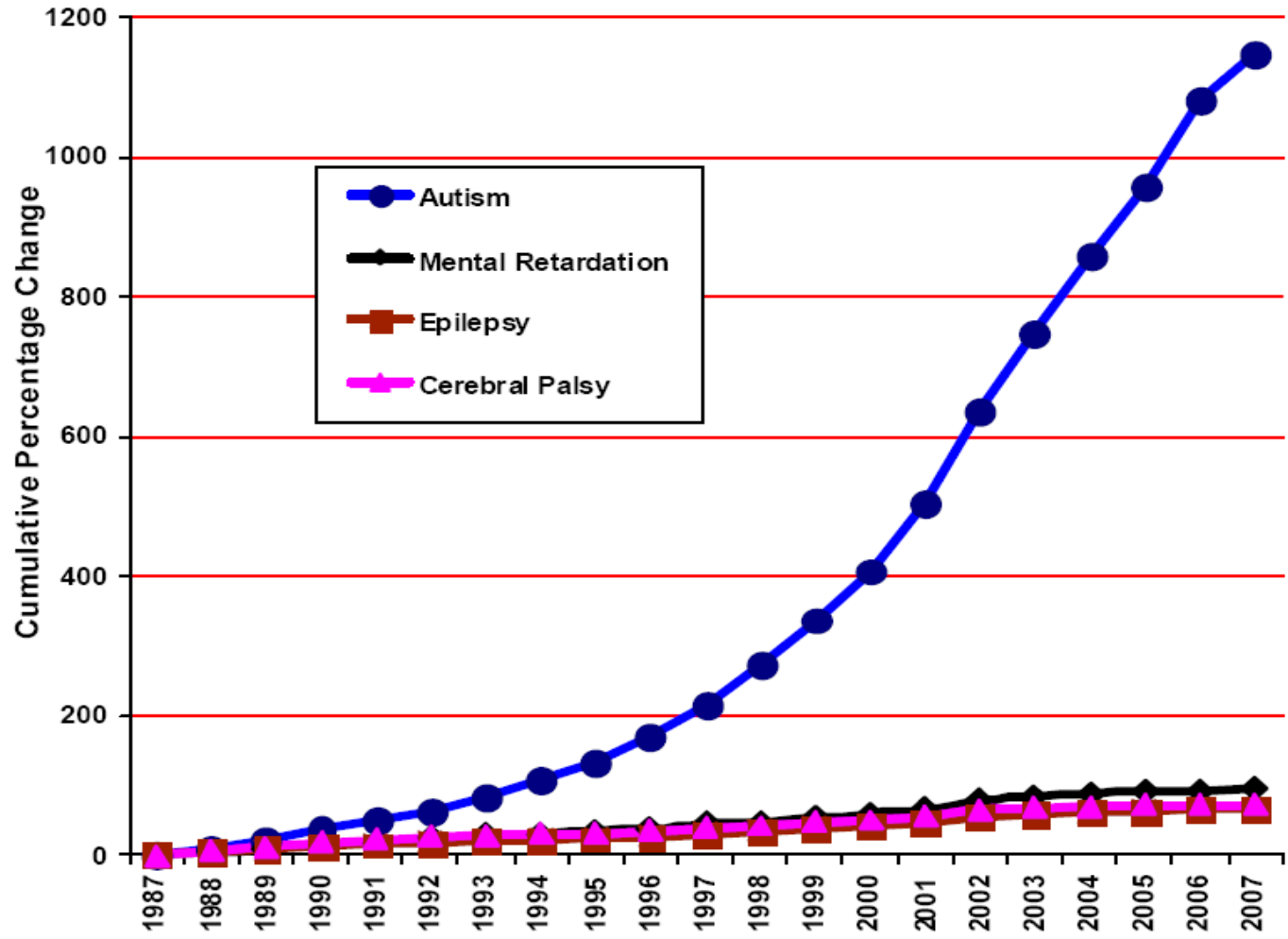
- ▶ 1 / 6 Australian children with mental health problem: depression, ADHD (1 / 6 in US)
 - ▶ Adolescents: depression 1 / 15, up to 1 / 4 with alcohol problems
 - ▶ 2 / 5 with alcohol problems (Ireland)
- 

Autism

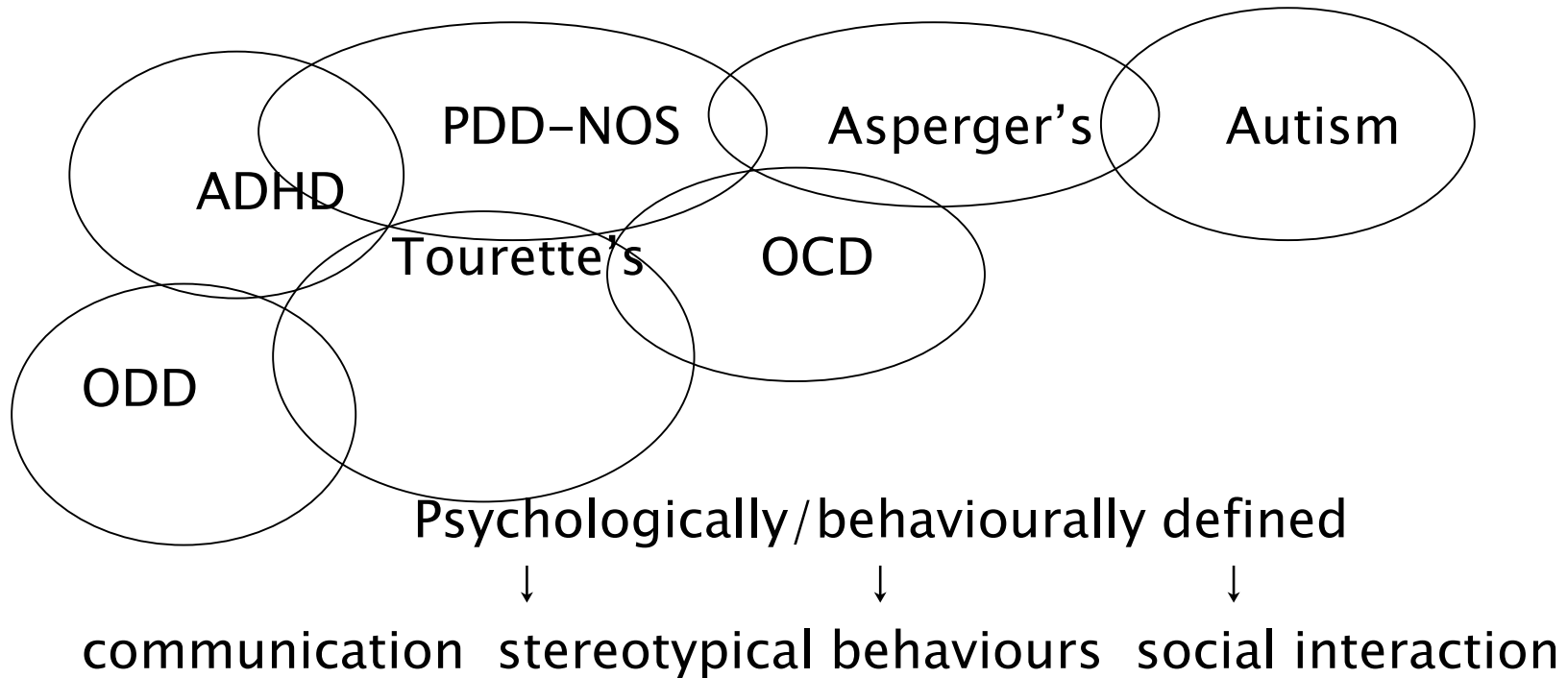
- ▶ (1985): 4 / 10,000
- ▶ (2001) 1 / 167
- ▶ (2007): 1 / 86
- ▶ (2011–2012): 1 / 50

Autism vs other developmental disabilities

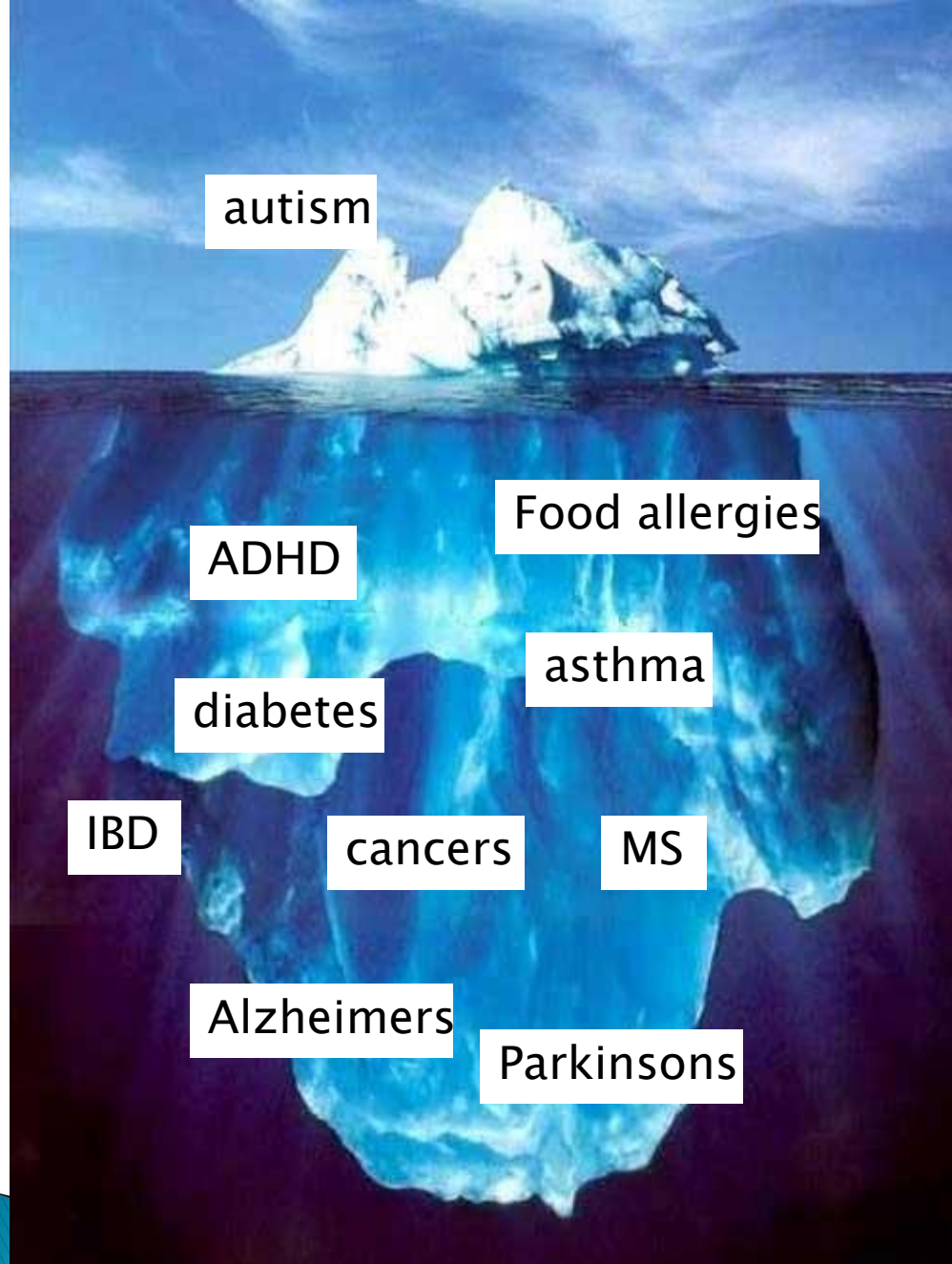
Figure 3: Cumulative Percentage Change of Autism, Cerebral Palsy, Epilepsy, and Mental Retardation over Two Decades



Overlapping Syndromes



Underlying pathophysiology:
biomedical problems?



autism

ADHD

Food allergies

asthma

diabetes

IBD

cancers

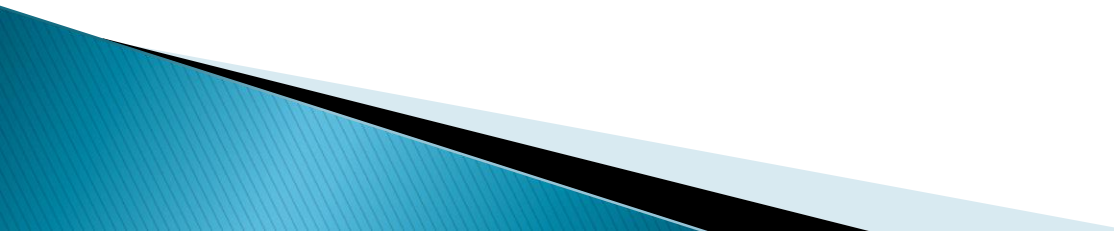
MS

Alzheimers

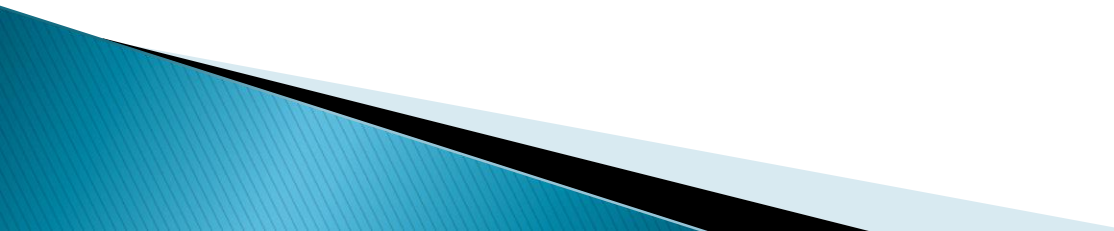
Parkinsons

Is autism
the tip of
an iceberg?

Autism– Not All in the Mind

- ▶ Abnormal brain function
 - ▶ Neuronal autoantibodies
 - ▶ Cross-reacting antibodies (strep, milk)
 - ▶ TH2 shift
 - ▶ Abnormal GALT – antibodies
 - ▶ Disturbed nutrition and metabolism
 - ▶ Is something happening in the gut?
- 

The Gut in Infants and Children

- ▶ Gastro-oesophageal reflux increasing in incidence in infants in recent years
 - ▶ Infant colic in nearly 50% western children
 - ▶ Incidence of juvenile Crohn's disease increasing
 - ▶ Gastroenteritis increasing: 2003–2004, 2 1/2x
- 

THE GUTS OF IT

“All diseases begin in the gut”

Hippocrates

Connections

80% immune system lines the gut: GALT

Gut bacteria determine state of immune system

Gut nervous system shares neurotransmitters with the brain

Connections between

- ▶ Food allergies and gut dysfunction
- ▶ Gut dysfunction and infection
- ▶ Food allergies, gut dysfunction, infections and neurodevelopmental, behavioural dysfunction

Gut-Brain Axis

- ▶ “gut-brain interactions may be central to abnormal neural development and the subsequent expression of aberrant behaviors”

Andrew Wakefield





A gut-brain link?



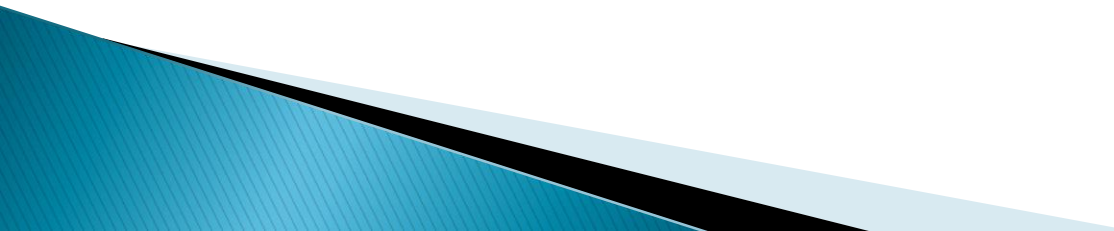
Many autistic children have abnormal levels of dysbiotic bowel flora.

Metabolites from bowel flora can affect behavior.

Chemical byproducts from incompletely digested food proteins can affect behavior.

Immune responses of gut wall to bacteria determines the state of the immune system

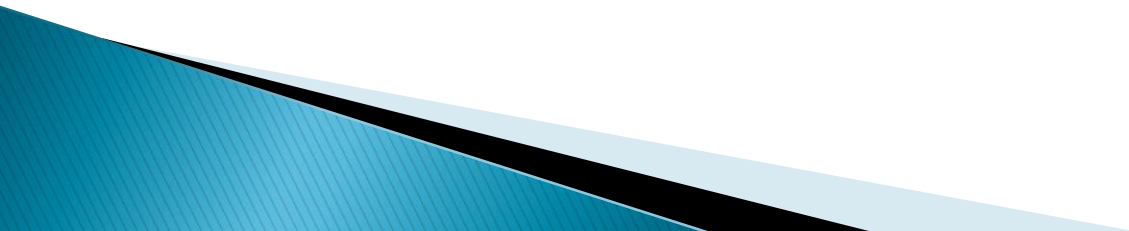
BRAIN–IMMUNO–GUT DISORDERS

- ▶ Increasing allergy, infections and immune disease
 - ▶ Increasing gastrointestinal dysfunction and disorders
 - ▶ Increasing neurodevelopmental, neurological and behavioural disorders
- 

WHY IS THIS HAPPENING?



IS IT ALL GENETIC?



Autism does not fit pattern for “classic” genetic diseases

▶ Classic disease

- Common in previous generations and extended family
- High risk in sibs and twins
- Prevalence decreases over time
- Sex ratio is usually 1:1 or 100% in one gender

▶ Autism

- Little background family history of autism: largely ‘horizontal’ inheritance
- Relatively low risk to sibs and twins
- Prevalence is increasing
- Sex ratio is 4:1 boys:girls

NO ONE GENE:

- ▶ Whole-genome screens in multiplex families suggest interactions of at least 10 genes

Maleness

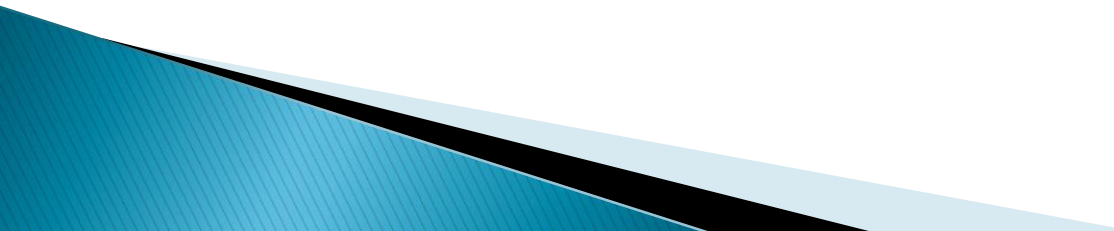
- ▶ Incidence of neurodevelopmental disorders (speech delay, behavioural difficulties, ADHD, autism) 3–4x that in females

- ▶ GENETIC 'RISK FACTORS'
- ▶ BUT:
- ▶ DOES HAVING THE GENES MEAN YOU WILL GET THE DISEASE?

Mutations and Disease Risk

- ▶ 2 114 year olds
- ▶ “The woman carried at least 30 mutations linked to Alzheimer’s disease, 201 mutations associated with cancer, 52 mutations associated with heart disease, 136 mutations associated with diabetes and 12 linked to macular degeneration that she was diagnosed with after the age of 100 years.
- ▶ The man carried 37 mutations associated with increased risk for colon cancer”. – he had had colon cancer in his 70s but lived an extra 40 years in excellent health
- ▶ (Perls T, *Frontiers in Genetics*, Jan 2012. New England Centenarian Study.)

Genetics and the Environment

- ▶ Genetics – genes stable: only changed 0.5% per million years
 - ▶ Environment: changed dramatically last century, particularly last 30 years
- 

Have we reached a toxic tipping point?

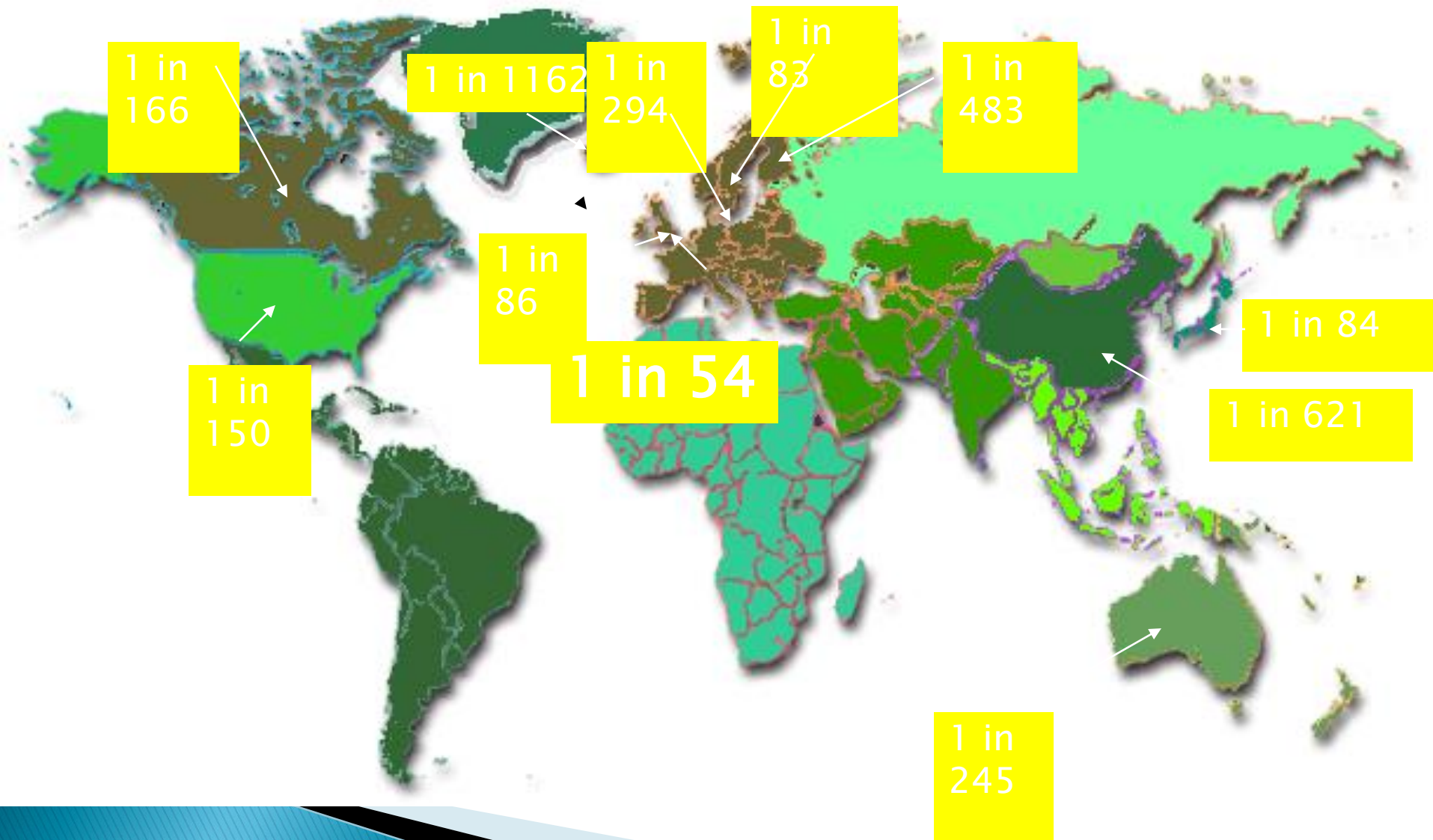


Epigenetics

- ▶ Environmental factors alter how genes 'read', resulting in apparent genetic change,
- ▶ Can be passed generationally

- ▶ GENES LOAD THE GUN
- ▶ ENVIRONMENT PULLS THE TRIGGER

Autism numbers are rising all over the world




Environmental

- ▶ 1004 autistic children : from developing Ethiopia to highly industrialised Israel
- ▶ rate PDD significantly lower in children immigrated from Ethiopia, higher in Israeli– born children.
- ▶ “may indicate that gestation, birth or infancy in industrialised countries exposes children to environmental insults that increase the risk for contracting PDD”

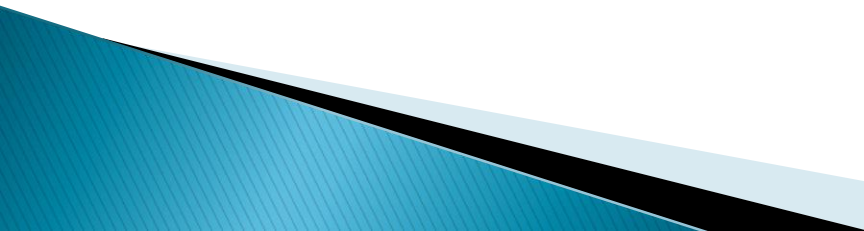
(Kmaer A et al. *Soc Psych & Psychiatr Epidem* 2004;39(2): 141–5)

- ▶ So what has changed in our environment in that time?

Environment

- ▶ Broader concept: anything external
 - ▶ Social: move from hunter-gatherer in tribes, to tribal agricultural, to agricultural village with communities, to extended families increasingly in cities, to nuclear families, to now, increasingly, single parent families
 - ▶ 2008 marked first year in history of man where there were more people living in cities globally than on the land
 - ▶ All other environmental changes can be considered as consequential to the social changes
- 

SOME MAJOR CHANGES

- ▶ Diet
 - ▶ Food growing, processing– chemicals
 - ▶ Environmental chemicals
 - ▶ Medical interventions – antibiotics, antipyretics, pharmaceuticals, anaesthetics, vaccinations
 - ▶ Pregnancy: older age, obesity, pregnancy complications, interventions
 - ▶ Childhandling practices, breastfeeding
 - ▶ Lifestyle factors
 - ▶ Electromagnetics
- 

DIET



Human Diet through History

human diet has passed through at least 4 phases

- 1 original diet (Garden of Eden): high in plant foods, leafy vegetables, shoots, roots, seeds, berries, fruit & nuts
- 2 hunting, herding – increased meat, dairy
- 3 agricultural – increased carbohydrates, cereals, legumes
- 4 supermarket phase – consumption highly processed foods, high in sugar, salt , saturated and trans-saturated fatty acids

(Dr Loren Cordain , 2006 CSIRO conference)

Modern Diet– Carbohydrates

- ▶ From time of industrial revolution onwards: around 1800
- ▶ introduction of refined sugar (sucrose), refined grains, high fructose corn syrup (HFCS)
- ▶ carbohydrates, grains up to 1/4 total energy
- ▶ 85% refined – most of high GI foods are refined cereal grains
- ▶ displaces minimally processed nutrient dense wild–plant, wild–animal foods

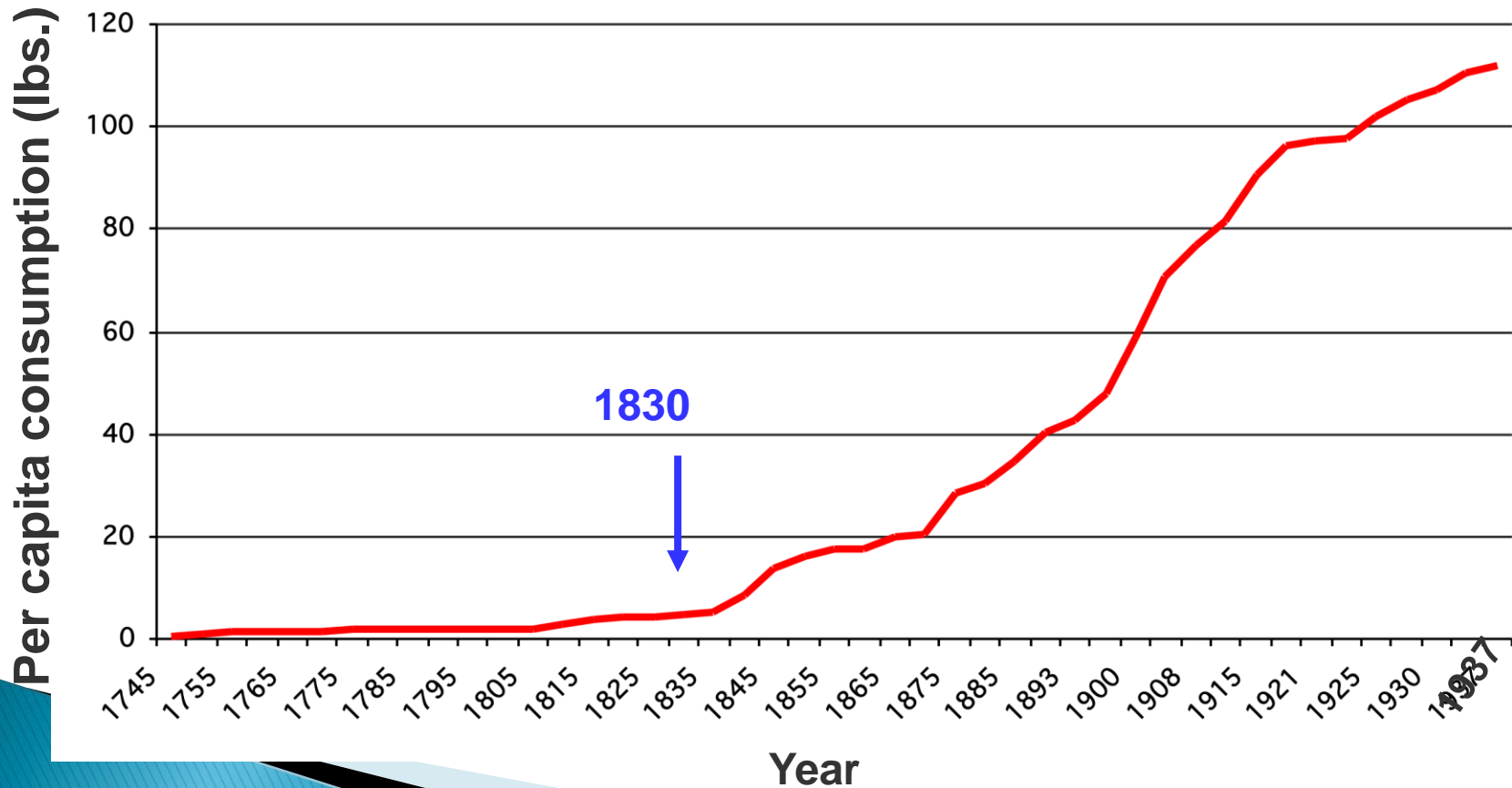
Modern Diet – EFA

From industrial revolution \uparrow omega 6 EFA, (20:1 omega 3) ,trans- fatty acids because:

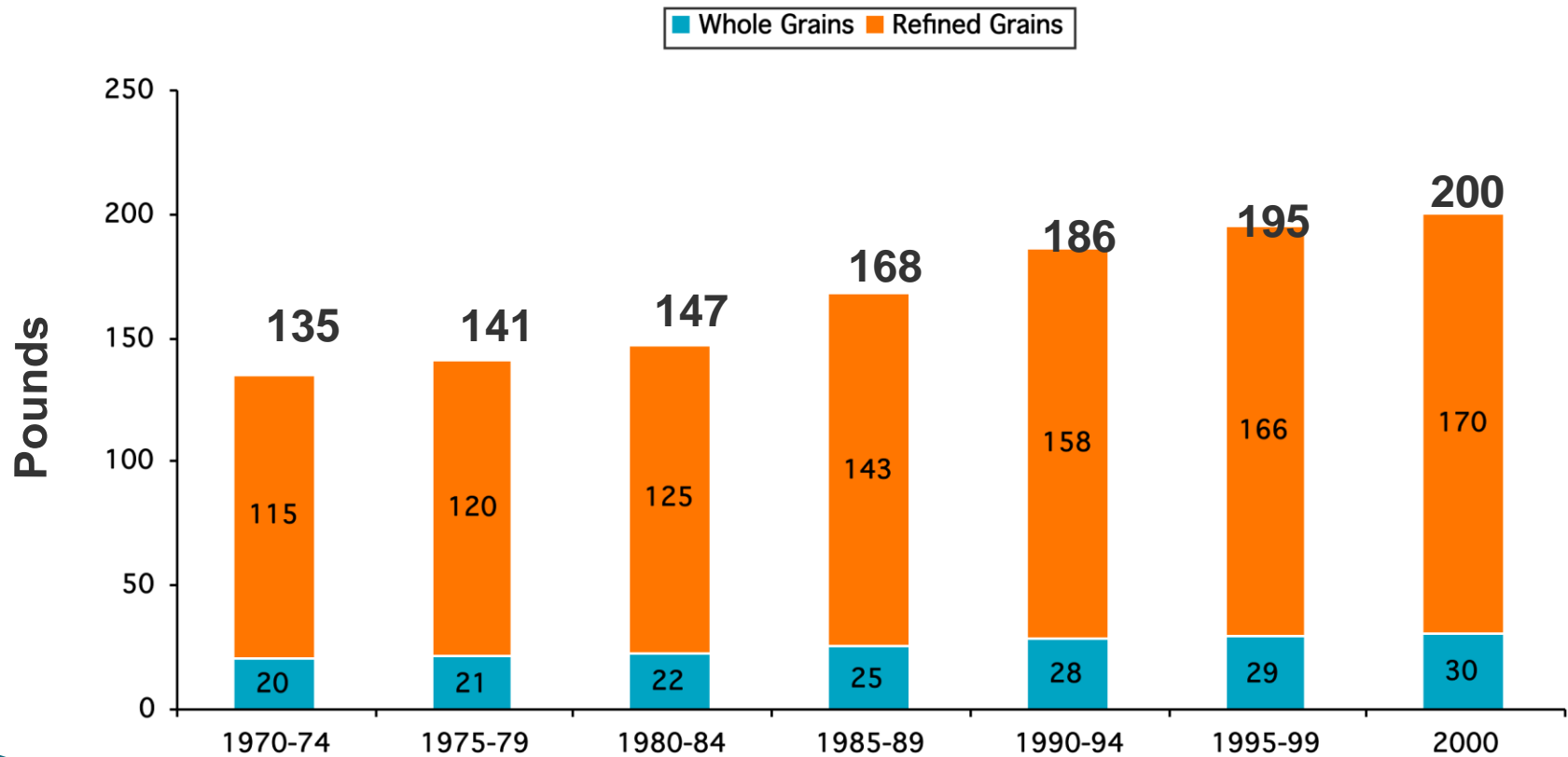
- ▶ hydrogenation of oils
- ▶ refined vegetable oils – especially soy oil– high omega 6
- ▶ \downarrow reduced game meats eaten
- ▶ domestic meats fed grain, feed –lots, \downarrow omega –3, \uparrow omega–6
- ▶ problem: xs omega–6 pro–inflammatory, TFA atherogenic (major risk factor for cardiovascular disease), depletion omega–3

Major Dietary Factors That Have Changed in the Past 200 Years?

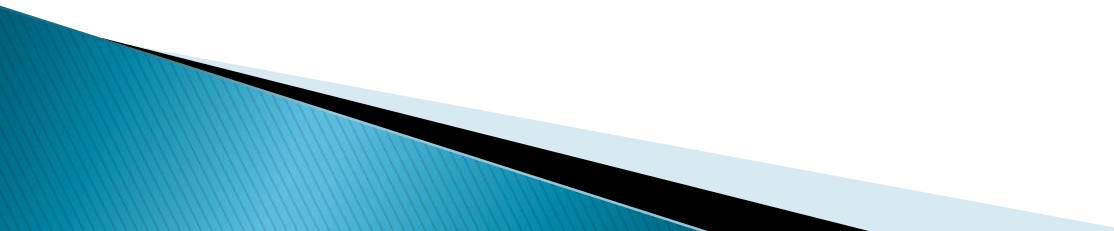
Per Capita Sugar Consumption (Glycemic Index = 65)
in the Netherlands (1745-1937)



Per Capita Consumption of Flours & Cereal Products in the U.S.

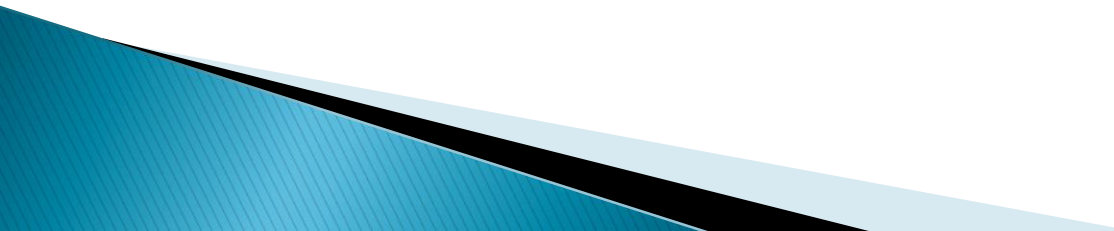


FOOD ADDITIVES

- ▶ Over 800 allowed food additives (NRA Aust 1998)
 - ▶ no register of what is actually ingested
 - ▶ food additives known problem years – Feingold diet
 - ▶ numerous studies
- 

Food Additives

- ▶ Recent UK studies: 2000 preschool children, older children
 - ▶ ‘We showed there was an effect on perfectly normal children’.
 - ▶ Follow up study in older children: effect also, although generally less than in younger

 - ▶ Britain’s Food Standards Agency issued immediate advisory to parents to limit intake of additives if they notice an effect on behaviour
- 

Chemicals

- ▶ 4 million chemicals listed, 80,000 regular use, <7% tested

(lecture Dr Stewart Lokkey, toxicologist, physician, author 'Invisible Killers 2007)

- ▶ As many as 3% of developmental and neurological deficits in children are caused by exposure to known toxic substances
- ▶ additional 25% of all developmental and neurological defects stem from environmental factors working in conjunction with genetic predisposition

(Nat Acad Sci June 2000)

Chemicals

- ▶ US companies annually report releasing into the environment 1.2 billion pounds of chemicals, “more than half ... are known or suspected developmental or neurological toxins”

(National Environmental Trust, Physicians for Social Responsibility, Learning Disabled Association of America “Polluting our Future: Chemical Pollution in the US that Affects Child Development and Learning” 2000, online)

- ▶ Umbilical cord blood now contains over 200 chemicals

▶ (EWG 2012)

A tsunami of chemicals, right under our noses

A Generation in Jeopardy
How pesticides are undermining
our children's health & intelligence



PESTICIDE ACTION NETWORK NORTH AMERICA

Pesticide Action Network
(PAN)

October 2012

Full scientific review of
hazardous pesticides in
farming use today

<http://www.panna.org/sites/default/files/KidsHealthReportOct2012.pdf>

PAN report summary (1 / 2)

1. Pesticide exposures cause harm to the structure and function of the brain and nervous system. Neurotoxic pesticides contribute to rising rates of ADHD, autism, declines in IQ and other cognitive dysfunction.
2. Pesticide exposures contributes to increasingly common health outcomes for children: birth defects, early puberty, certain child hood cancers.

PAN report summary (2/2)

3. Emerging science shows pesticide contribution to current epidemic of childhood asthma, obesity and diabetes.
4. **EXTREMELY LOW LEVELS** of pesticide exposure can cause significant health harms, **PARTICULARLY DURING PREGNANCY AND EARLY CHILDHOOD.**

Where are these chemicals found ?

- ▶ All conventionally farmed food
- ▶ Fragrances and perfumes
- ▶ Preservatives
- ▶ Anti- perspirants (with aluminium)
- ▶ Detergents: shampoo, bubble bath, shower gel
- ▶ Head lice treatment
- ▶ Sunscreen
- ▶ Flouridated toothpaste
- ▶ Make-up
- ▶ Hair dyes
- ▶ Food wrapped esp heated in plastic
- ▶ Dry cleaning
- ▶ Washing powders and softeners
- ▶ New clothes / curtains / carpets / furniture
- ▶ Seafood (methylmercury)
- ▶ Building materials, paints, solvents, sealants

And where else?

- In food...
- In bodies and breast milk
- Less in organically grown produce and fed animals
- Much more in any processed food

Goldman LR. Chemicals and children's environment: what we don't

Know about the risks. Environ Health Perspect 1998; 106 (suppl3): 875-880

Woodruff et al. Environmental chemicals in pregnant women in the United

States: NHANES 2003-2004. Environ Health Perspect 2011; 119: 878-885

- Also everywhere else:
- Millions of consumer products
- All household, cleaning, perfume, cosmetics, toiletries
- Furnishings, leather, clothes...

PREGNANCY, INFANCY

Maternal Heavy Metals

- ▶ CDC (USA) 10% women child-bearing age raised hair and blood mercury (MMWR Morb Mort Wkly Rep 2004;53(43)1018-20)
- ▶ Maternal mercury levels correlate with number of amalgams (Huojel PP, *AM J Epidem* 2005;161(8):734-40)
- ▶ Foetal death can be associated with high tissue mercury levels correlating with number of maternal amalgams (Drasch,G et al, *Europ J Pediatr* 1994;153:607-10);

Infancy– Child–handling Practices

- ‘normal’ to cry for 3 hours per day at age 6 weeks in Western society
- tribal societies in Africa, Pacific Islands carry babies all day, and a village with 100 babies may not have a single baby who cries;

“This system is not convenient to Western mothers”

(Gurry D, *Inconsolable Babies:the shadowy syndrome of three months’ colic,Modern Medicine 42;5:26–32.*)

- ‘Controlled crying’ favoured form of management of infantile sleep difficulties
Australian society
- told to “resist comforting a crying baby so it can teach itself to go to sleep” . (Simon B, as reported in *Medical Observer* 14 May 1999)

Infancy–Child–handling Practices

- ▶ Babies given greater physical stimulation by way of bathing, exercising, being taken out of capsule or cuddled show significant improvement in motor skills at about 4th month age – 4th month recognised as critical time child development (Bridgewater KJ, Sullivan MJ et al. ‘*Wakeful positioning and movement control in young infants: a pilot study*’. *Aust J Physio* 1999;45:259–66).

Vaccination– WHO

- ▶ Vaccination induces immune system shift from TH1 (native immunity) to Th2 (Allergy, antibody–dependant immunity)
- ▶ Predominance Th2– biased pattern with impaired induction of cytotoxic T cells in response to vaccines in neonates and early life as compared to adults (mice).
- ▶ Effect did not disappear with aging and was still reflected in adult responses to booster immunisation.

(Barrios C et al, Eur J Immunol 1996 Jul;26(7):1489–96. WHO Collaborating Centre for Neonatal Vaccinology, University of Geneva, Switzerland).

Vaccination and Neurodevelopmental Disorders

- ▶ 2001–2007, USA
- ▶ Positive correlation between the proportion of children who received vaccinations and the incidence of autism or speech and language impairment .
- ▶ For each 1% increase in vaccination rate, 680 additional children were diagnosed with autism or speech delay.
- ▶ Not proof of an effect but an association
- ▶ DeLong, G. A positive association found between autism prevalence and childhood vaccination uptake across the U.S. population. *J. Toxicol. Env. Health A* 2011, 74, 903–916.

Antibiotics

- ▶ Marked alterations in gut bacteria
- ▶ 25% – antibiotic-related diarrhoea
- ▶ May be evident 1 year later after single dose
- ▶ Multiple courses may alter gut bacteria permanently
- ▶ Use in children and infants increases the risk of immune shift and asthma
- ▶ Effects on immunity in children can be longstanding
- ▶ Reduction in beneficial phytoestrogens eg enterolactone

PARACETOMOL

- ▶ Routinely used to control fever in infection, vaccinations
- ▶ Results in depletion of n-acetyl cysteine, required for synthesis of glutathione, major intracellular antioxidant
- ▶ Use of paracetamol in the first year of life and in later childhood, is associated with risk of asthma, rhinoconjunctivitis, and eczema at age 6 to 7 years.
- ▶ The Lancet, Volume 372, Issue 9643, Pages 1039 – 1048, 20 September 2008

Paracetamol, Vaccines and Autism

- ▶ **Acetaminophen (paracetamol) use, measles–mumps–rubella vaccination, and autistic disorder. The results of a parent survey**
- ▶ -83 children with autistic disorder and 80 control children.
- ▶ paracetamol use after MMR vaccination in children 5 years of age or less, 6x risk autism
- ▶ children with regression in development 4x risk
- ▶ children who had post–vaccination sequelae– 8x risk
- ▶ Autism May 2008 vol. 12 no. 3 293–307. Stephen Schultz et al.

Anaesthetics

- ▶ Study over 2600 children WA
- ▶ Exposure to anaesthetic before age 3 years
- ▶ 2x risk development clinically significant language impairment, to have problems with abstract reasoning by age 10
- ▶ Paediatrics 2012: 130:e476-485

Infections, Reflux, PPI's

- ▶ Use of PPI in infancy for GORD and increased rates of gastroenteritis (2x, to 50% children) or pneumonia (5x, to 12%)

(*Peds* 2006;117:817-820)

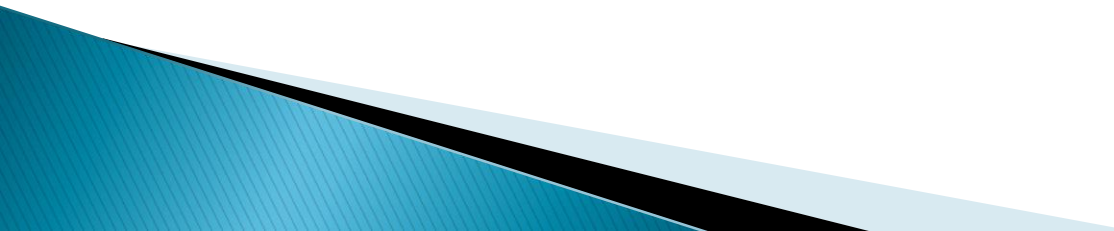
- ▶ PPI also linked with 3x *clostridial difficile* associated disease (CDAD) (*JAMA* 2005)
- ▶ PPIs induce hypochlorhydria

As a Consequence:

- ▶ “Longevity declining in the next generation”
“There is concern, and a lot of literature to support it, that there will be a generation of children who will die before their parents. They will be so fat that they will develop diabetes, cancer, heart disease – there’s an endless list. From Cardiff and Vale University Health Board statistics *As reported by walesonline.co.uk on January 15, 2012.*

'The Whole of Creation Groans'

- ▶ Environment crisis – resources, loss species, pollution
- ▶ Population crisis
- ▶ Health crisis – 1 / 2 obesity, 1 / 2 cardiovascular disease, 1 / 2 cancer (males), 1 / 3 Alzheimer's disease, 1 / 3 mental disease;
- ▶ Peak longevity – those born before WWII– now reversing
- ▶ Children: 1 / 2 allergy, 1 / 4 asthma, 1 / 10 ADHD, 1 / 10 learning difficulty, 1 / 50 autism
- ▶ First time in recorded history: our children will die before us

- ▶ URGENT NEED TO BE RESTORED:
 - ▶ TO CONNECTION WITH THE CREATION:SIMPLE OUTDOORS LIFETYLE, ACTIVITY
 - ▶ TO FOODS AS FOODS USED TO BE PRIOR TO THE INDUSTRIAL REVOLUTION
 - ▶ TO EACH OTHER:COMMUNITY
- 

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