Immune Disease and the Microbiome:
PPPM Healthcare in response to New Knowledge

Trevor G Marshall,

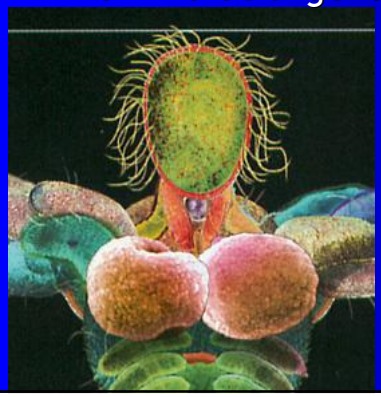
Autoimmunity Research Foundation, California

revised: 5 Sept 2016

Source:
www.NAU.edu

No, *THIS* Microbiome

"Man is a Superorganism"
25,000 Human Genes
>1 million microbial genes



NewScientist Health

Babies are born dirty, ~~with a gutful of bacteria~~

› Updated 15:33 12 April 2012 by **Jessica Hamzelou**
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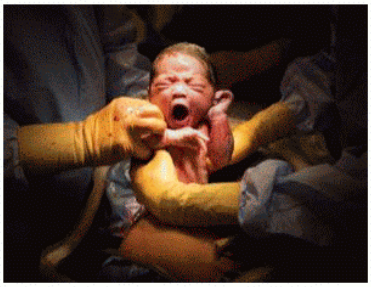
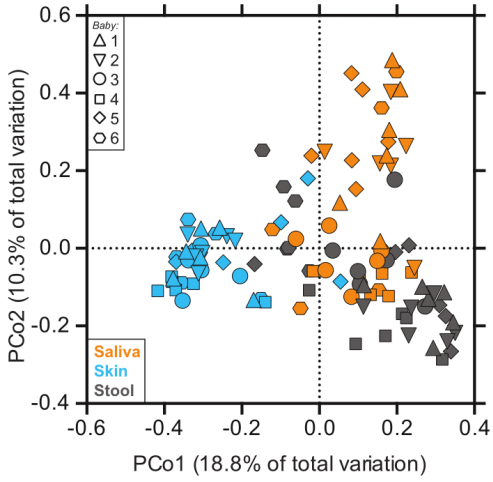
IT HAS long been assumed that the fetus lives in a sterile world, protected from the countless bacteria that fill its mother's gut and cover the surface of her body. A baby's first gut flora was thought to be collected at birth - either from the mother's vagina or from the environment it is born into. But it's time for a drastic rethink: it appears that we are in fact born dirty - bacteria colonise our guts in the womb, where they begin to shape our immune systems and influence our risk of disease. What's more, this collection of bacteria, or microbiome, could eventually be manipulated to ensure a baby is given the healthiest start in life.

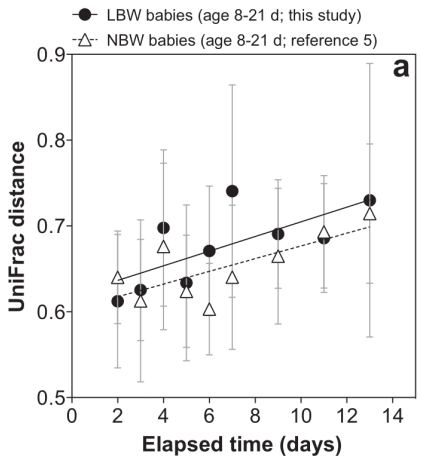
Some of the first evidence that mammals might begin to develop a microbiome before birth came from studies in mice published four years ago.

Esther Jiménez and her colleagues at the Complutense University of Madrid, Spain, labelled bacteria with a genetic marker and fed milk containing them to



The baby's had visitors already *(Image: Richard Schutz/Corbis)*

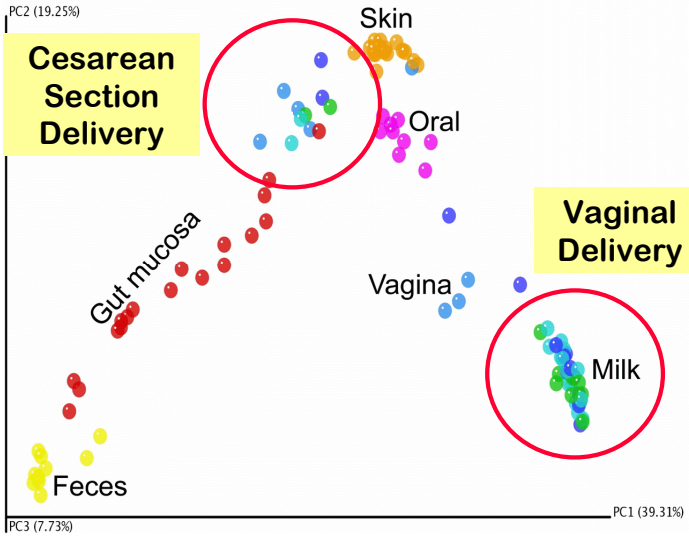




Unweighted UniFrac-based principal coordinate analysis (PCoA) of LBW infant-associated bacterial communities

Dave Relman's group: Costello EK, et al: *Microbiome Assembly across Multiple Body Sites in Low-Birthweight Infants.* MBio. 2013 Oct 29;4(6)

Human Breast Milk Microbiome



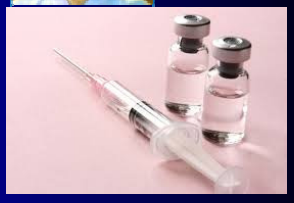
Hypervariable regions V1 and V2 of the 16S RNA gene of bacteria in human breast milk.

Raul Cabrera-Rubio, et al: The human milk microbiome changes over lactation and is shaped by maternal weight and mode of delivery. American Journal of Clinical Nutrition, Jan 2013.

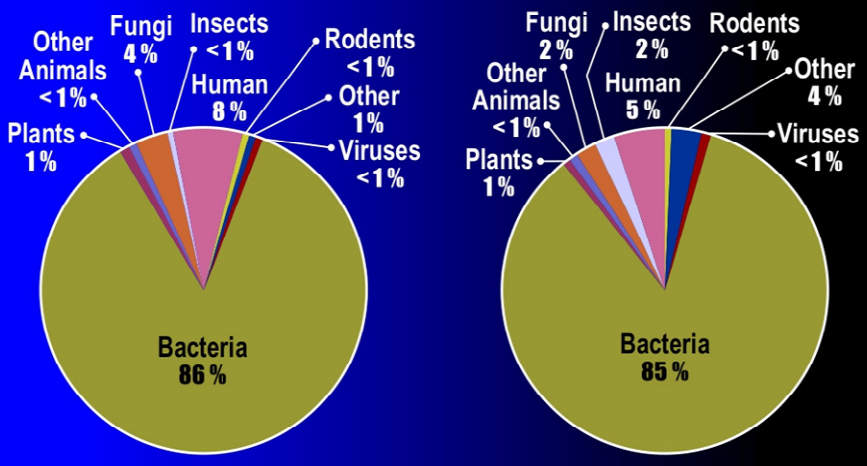
Our Microbiome grows from our Environment

From our pets, family and friends

From Travel, Food, and Medicines



Types of Organisms in Air Samples:



San Diego Indoor Hospital

San Diego Indoor House

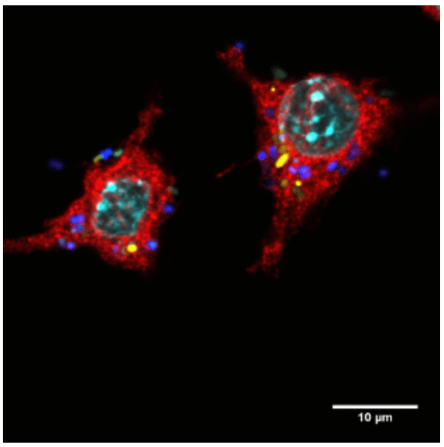
SOURCE: J. CRAIG VENTER INSTITUTE 2012

TheScientist
EXPLORING LIFE, INSPIRING INNOVATION

How Bacteria Evade the Immune System

***Escherichia coli* can quickly evolve to resist engulfment by macrophages, scientists have found.**

By Laasya Samhita | December 12, 2013



Bacteria exposed to antibiotics rapidly acquire mutations that allow them to develop resistance to the drugs, and this process is fairly well understood. Scientists have now looked at the evolution of bacterial resistance toward live agents: cells of the immune system. In a report published in *PLOS Pathogens* today (December 12), a team led by Isabel Gordo from the Instituto Gulbenkian de Ciência in Oeiras, Portugal, challenged the common human intestinal bacterium *Escherichia coli* with mouse macrophages—immune system cells that engulf foreign elements like bacteria—and observed the rapid evolution of mutants capable of escaping capture. The same *E. coli* mutants could successfully establish infections in mice.

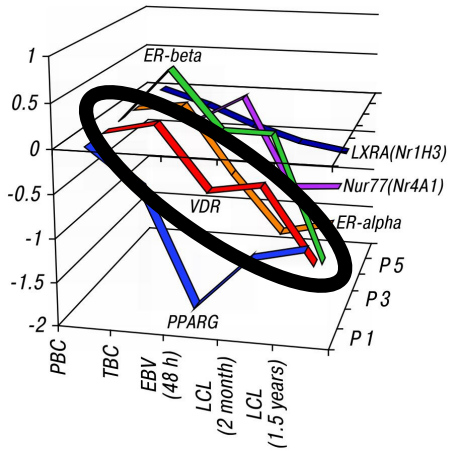
M. Miskinyte et al., "The genetic basis of Escherichia coli pathoadaptation to macrophages," PLOS Pathogens, 9(12): e1003802, 2013.

VDR / Innate host defenses are key

In order to survive inside human phagocytic cells, microbes have had to evolve to knock out the VDR -- so that they don't have to deal with the cell's innate defenses

In *Homo sapiens*, and only in *Homo sapiens*, one Nuclear Receptor, the VDR, expresses genes for TLR2, as well as the Cathelicidin and beta-Defensin anti-microbial peptides, all of which are essential to intra-cellular innate immune defenses.

Pathogens Downregulate VDR Nuclear Receptor



(Yenamandra SP, et al: *Exp Oncol* 2009,31,2)

Persistent EBV down-regulates VDR more than 10 fold.

Note that the most pronounced effect is in the immature lymphoblastoid cell lines (LCL) after 1.5 years of exposure

Species Known to act on VDR:

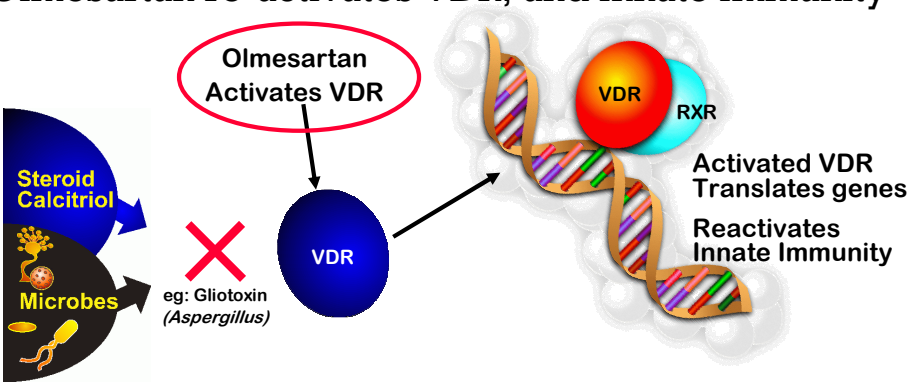
Mycobacterium tuberculosis,
Aspergillus fumigatus,
Borrelia burgdorferi,
Chlamydia trachomatis,
HCV, CMV and EBV

→ Immuno-stimulation,

not Immuno-suppression

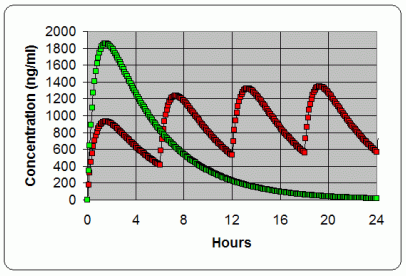
Inflammation is a body's healing-response. It is not, of itself, something inherently bad which needs to be suppressed at all cost

Olmesartan re-activates VDR, and Innate Immunity



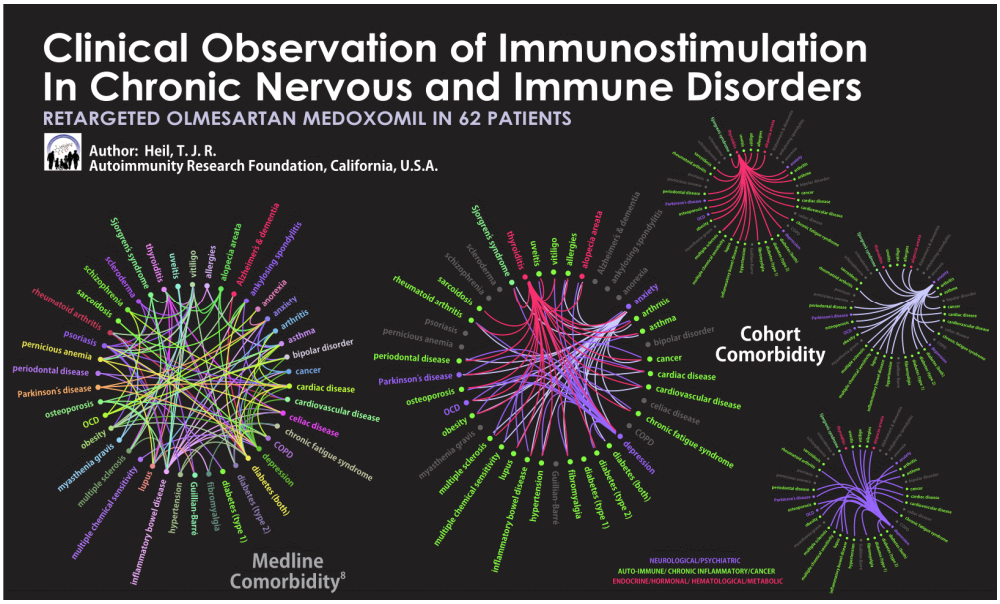
INPUT

D [mg]	40	80
tau [h]	6	25
n	4	1
t1/2abs[h]	0.47	0.47
Vd [L]	31	31
CL [L/h]	6.66	6.66

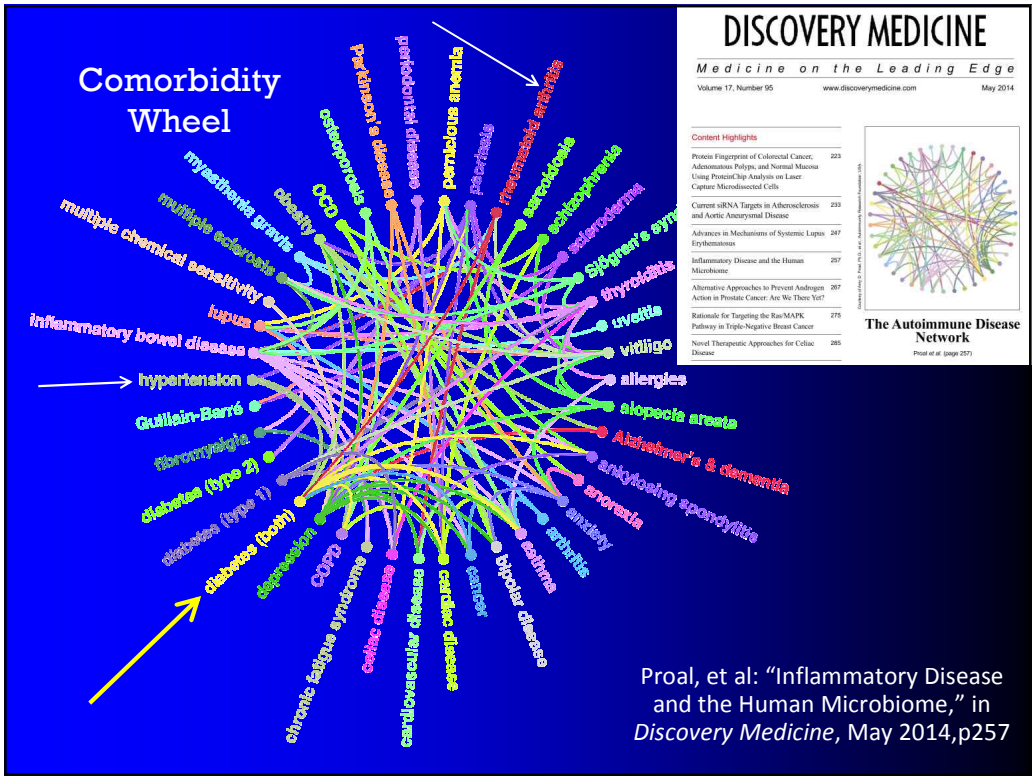


OUTPUT

Peak(ss)	1355	1868
Trough(ss)	574	14
tmax(ss)[h]	1.3	1.5
Cave	1001	480
ke [1/h]	0.21	0.21
ka [1/h]	1.5	1.5
t1/2(el) [h]	3.2	3.2
F	2.4	132.4
r	1.4	1.0



Trudy Heil, MS, ARNP, CLNC: Poster Presented at 5th Intl. Symp. on the "Interaction of Nervous and Immune Systems," RAMS, St Petersburg, 2015



ВЕСТНИК
САНКТ-ПЕТЕРБУРГСКОГО УНИВЕРСИТЕТА
Серия 11 | 2013 | МЕДИЦИНА
Выпуск 3 | Сентябрь

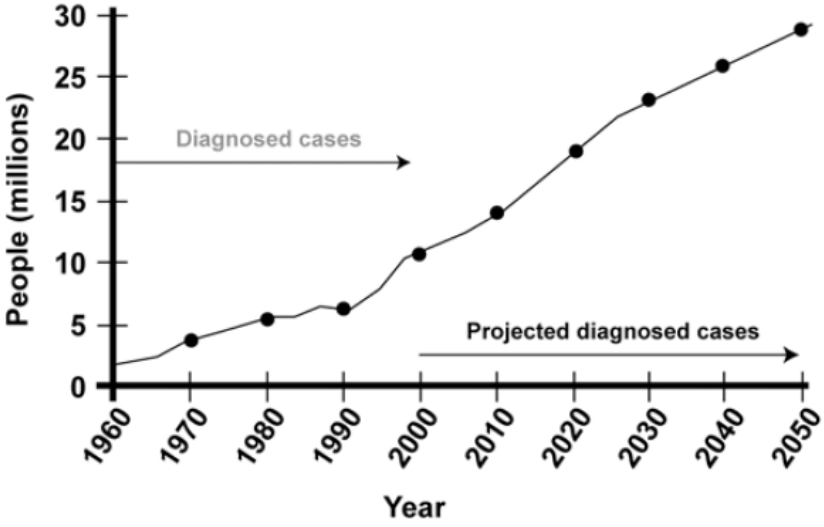
T. G. Marshall

"THE SCIENCE OF SAFETY" — IS IT REALISTIC TO EXPECT MEDICINE TO CHANGE TO A SCIENCE-BASE FROM ITS EVIDENCE-BASE?

Introduction. A century ago, Max Planck's autobiography described the pace of scientific change: "A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it" [1]. Today, as Medical Science struggles to assimilate discoveries springing from the decoding of the Human Genome, two obvious questions arise — "how long will it take for this new Genomic Science to take hold in general medical practice?" and "will this be fast enough to keep pace with the epidemic proliferation of chronic disease?"

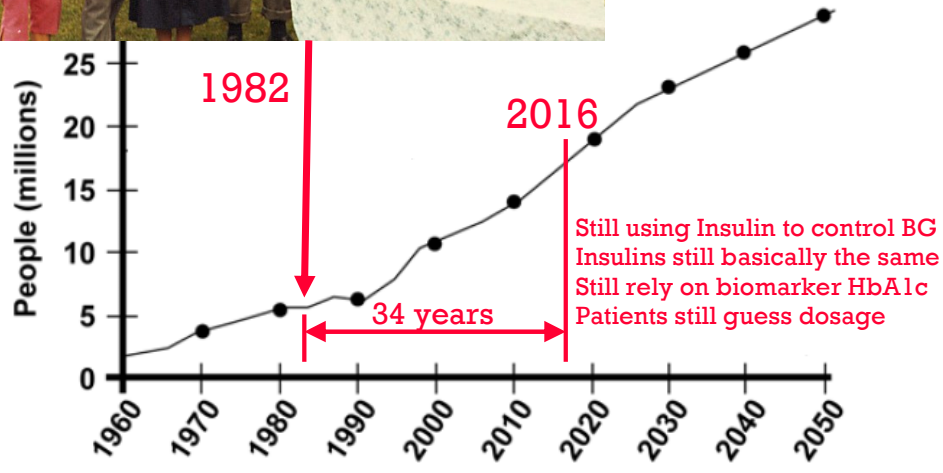
Science often gives answers you did not want

PPPM: Projected Prevalence of Diabetes (CDC USA)



SOURCE: Data for 1960–1998 from the National Health Interview Survey, National Center for Health Statistics (NCHS). Centers for Disease Control and Prevention (CDC) projected data for 2000–2050 from the Behavioral Risk Factor Surveillance System, Division of Diabetes Translation, CDC.

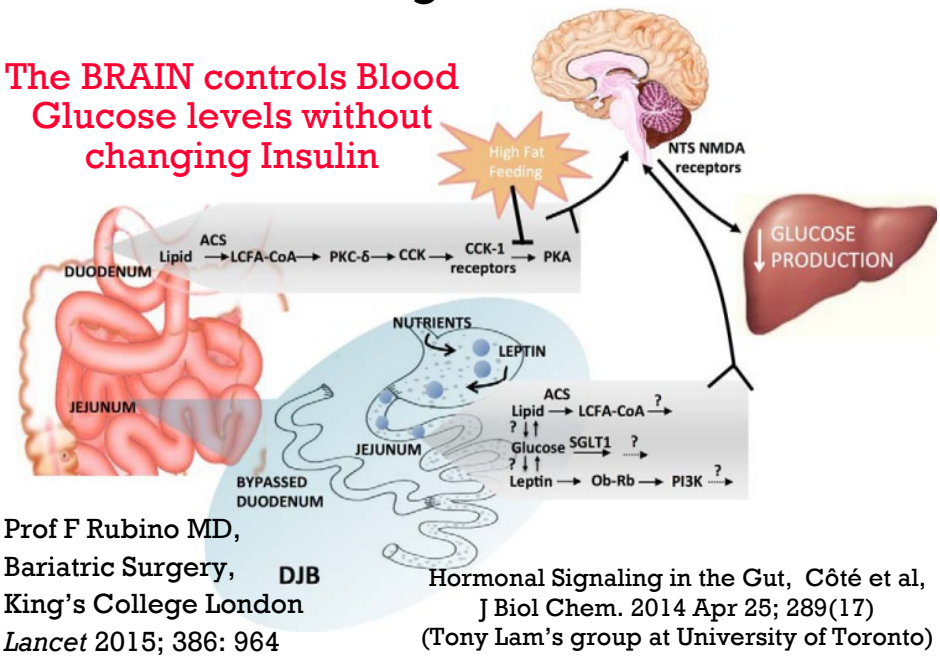
Diabetes Research Group,
Dept of Surgery,
Hospital for Sick Children,
Toronto, 1982



Still using Insulin to control BG
Insulins still basically the same
Still rely on biomarker HbA1c
Patients still guess dosage

New Knowledge about Diabetes

The BRAIN controls Blood Glucose levels without changing Insulin



Prof F Rubino MD, Bariatric Surgery, King's College London
Lancet 2015; 386: 964

DJB

Hormonal Signaling in the Gut, Côté et al, J Biol Chem. 2014 Apr 25; 289(17)
(Tony Lam's group at University of Toronto)

JAMA The Journal of the American Medical Association

February 23, 2011, Vol 305, No. 8 >

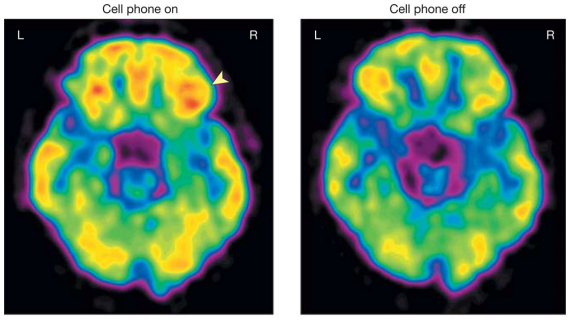
Preliminary Communication | February 23, 2011 *JAMA*. 2011;305(8):808-813. doi:10.1001/jama.2011.186.

Effects of Cell Phone Radiofrequency Signal Exposure on Brain Glucose Metabolism

Nora D. Volkow, MD; Dardo Tomasi, PhD; Gene-Jack Wang, MD; Paul Vaska, PhD; Joanna S. Fowler, PhD; Frank Telang, MD; Dave Alexoff, BSE; Jean Logan, PhD; Christopher Wong, MS

[-] Author Affiliations

Author Affiliations: National Institute on Drug Abuse, Bethesda, Maryland (Dr Volkow); National Institute on Alcohol Abuse and Alcoholism, Bethesda (Drs Volkow, Tomasi, and Telang and Mr Wong); and Medical Department, Brookhaven National Laboratory, Upton, New York (Drs Wang, Vaska, Fowler, and Logan and Mr Alexoff).



Rate of glucose metabolism,

EASD European Association for the Study of Diabetes

Immunologic Research

pp 1–7

Electrosmog and autoimmune disease

Trevor G. Marshall ✉, Trudy J. Rumann Heil

Open Access | Environment and Autoimmunity

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1.4k Views

Microwave Electrosmog (TV,WiFi, CellPhones)

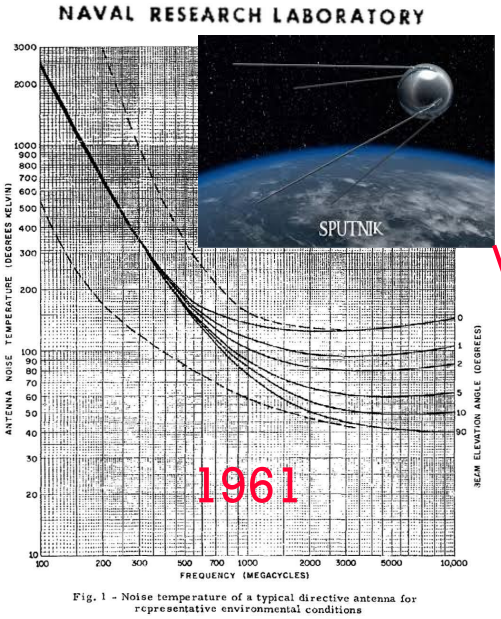
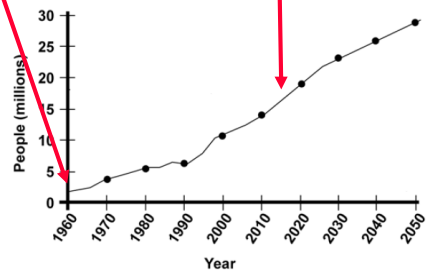


Fig. 1 - Noise temperature of a typical directive antenna for representative environmental conditions

2016 Electrosmog levels 50,000 times greater



World Health Organization

Media centre

New WHO report: deaths from noncommunicable diseases on the rise, with developing world hit hardest

Noncommunicable diseases a two-punch blow to development

News release

27 APRIL 2011 | MOSCOW - Noncommunicable diseases are the leading killer today and are on the increase, the first WHO *Global status report on noncommunicable diseases* (NCDs) launched today confirms. In 2008[1], 36.1 million people died from conditions such as heart disease, strokes, chronic lung diseases, cancers and diabetes. Nearly 80% of these deaths occurred in low- and middle-income countries.

It may not be possible for true PPPM breakthroughs without fundamental changes to existing models for Healthcare, Medicine and Science