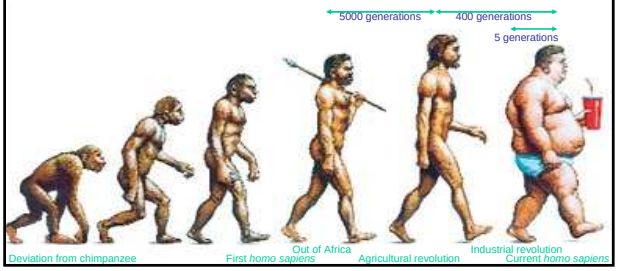
The evolutionary origin of Western disease

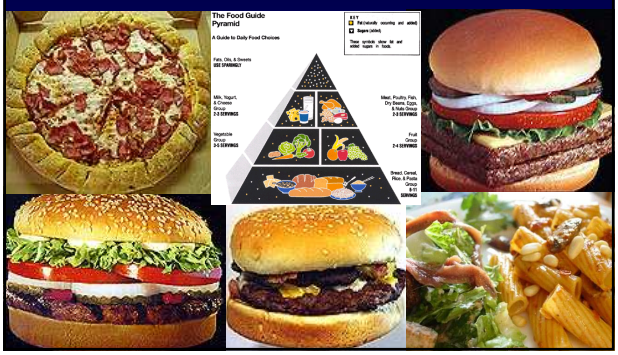
Frits A.J. Muskiet

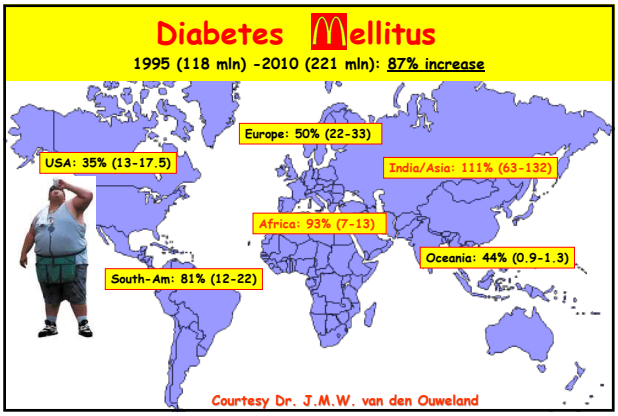
Laboratory Medicine, University Medical Center Groningen

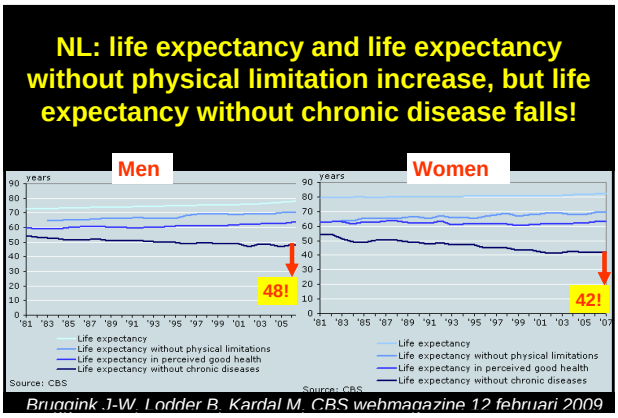


Why is this funny?

And why is this 'normal'?

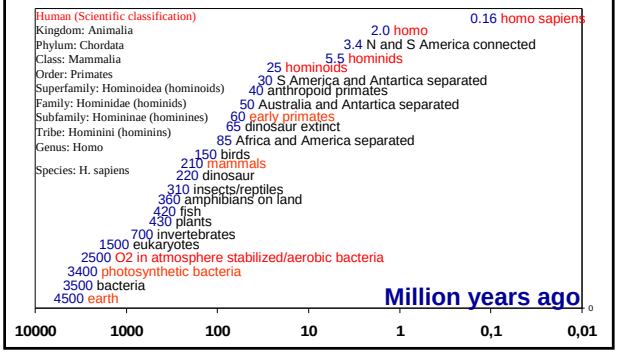


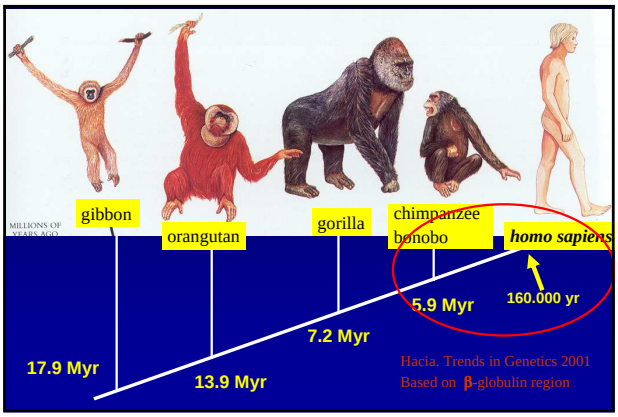


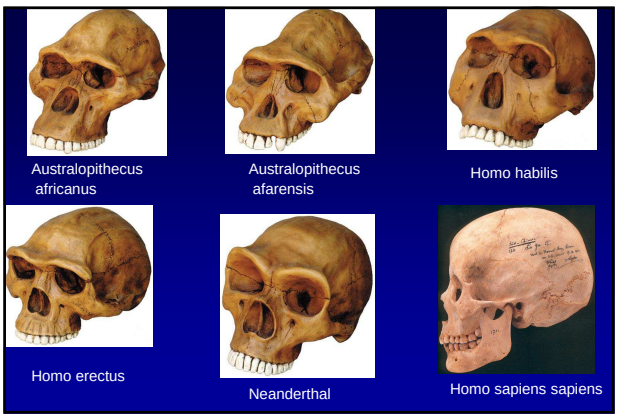


Om het heden te begrijpen moet men het verleden kennen

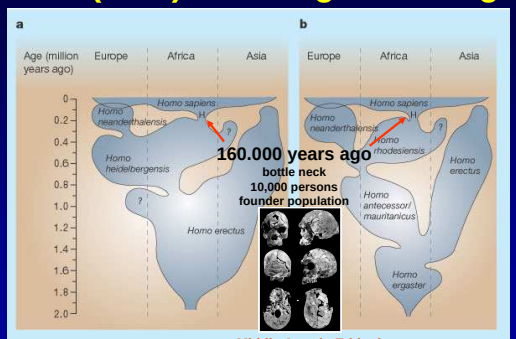
Earth biological and geographic evolution







Out of (East) Africa again and again



Stringer, Nature 2003

Middle Awash, Ethiopia
White, Nature 2003

160,000 years old *H. sapiens idaltu*

from Herto, Middle Awash, Ethiopia

White, Nature 2003; Gibbons, Science 2003

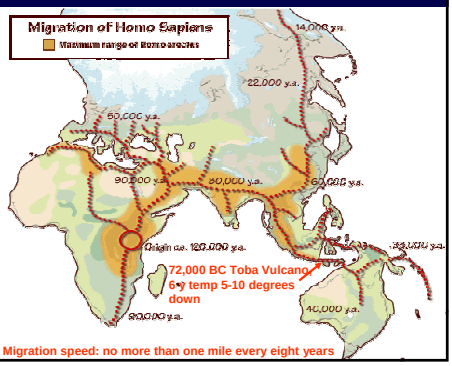
Reconstruction:
www.dienekes.com/blog/archives/cat_physical_anthropology.html

We are of East African ancestry: 3rd Out of Africa wave

Genetic diversity highest among Africans

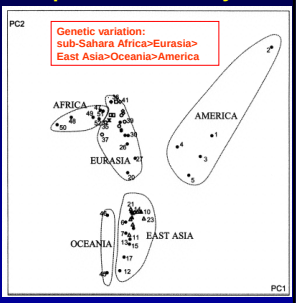
Adaptation to local conditions

- Mutation.
- Gene flow (no admixture).
- Genetic drift /bottle necks (small populations



Migration speed: no more than one mile every eight years

‘Race’ is biologically meaningless. ‘Out of Africa’ predicts more genetic homogeneity in the geographic region of origin of a person’s ancestry



Microsatellite clustering of 52 world-wide populations Zhivotovsky Am J Hum Genet 200

Do we people still adapt genetically?

Candidate gene	Hypothesized selective pressure
Lactase persistence	improved nutrition from milk
G6PD	protection malaria
Duffy blood group	protection malaria
HbC (Mossi, N-Ghana, -1000 y)	protection malaria
TNFSF5	protection malaria
CCR5 (-700 y)	protection smallpox, HIV
H2 haplotype	? but only in Europe
DRD4	cognition, behavior
MAO- A	cognition, behavior
AGT	protection hypertension
CYP3A	protection hypertension
TAS2R38	bitter taste perception

Balter, Science 2005

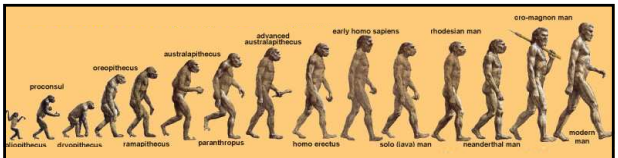
So, what went wrong?

The background of typically "Western" disease is not genetic!

Less than 5% of major CA and CAD is 'merely' genetic

(i.e. derives from highly penetrant germline mutations)

Willett, Science 2002

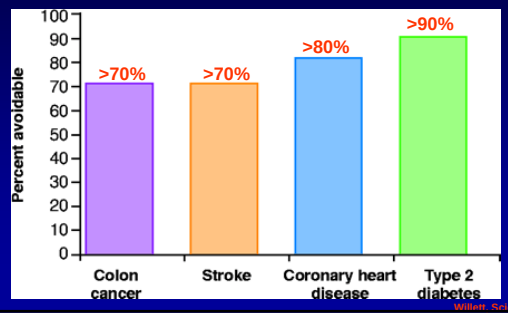


Our genome is perfect since it is the result of millions of years of evolution

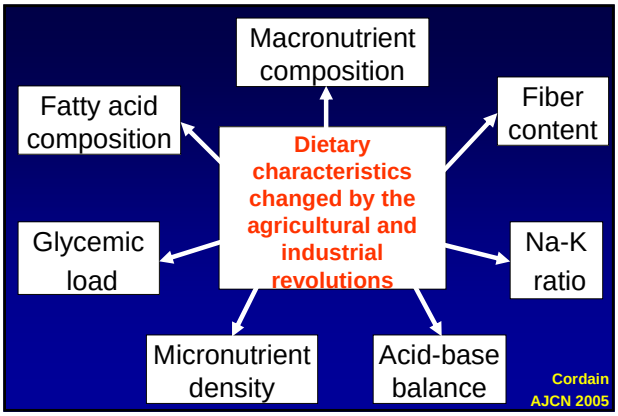
It changes with 0.5% per million years

Environmental influences on major diseases

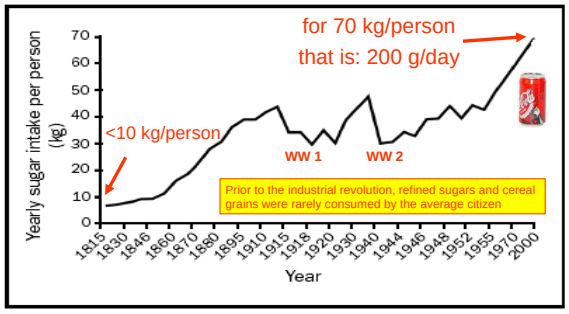
PARs for lifestyle (here: specific aspects of diet, overweight, inactivity, smoking)



Willett, Science 2002

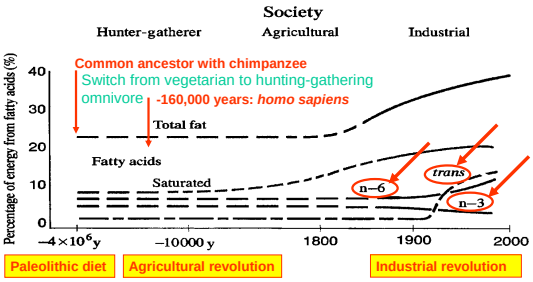


UK/US yearly sugar consumption
1815-2000



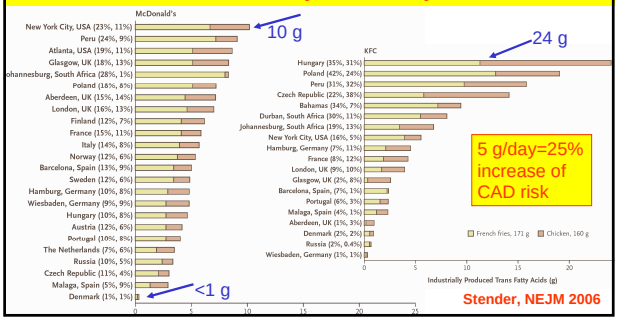
Keefe, Cordain. Mayo Clin Proc 2004

Fat intake of hominids and *homo sapiens*



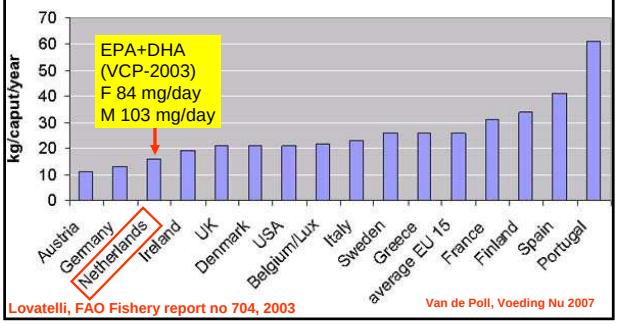
Simopoulos, AJCN 1999

Industrially produced trans fatty acids in a large serving of fast food from two outlets in various countries (2004-2005)



Stender, NEJM 2006

Fish consumption in EU and USA 1994-1998



Lovatelli, FAO Fishery report no 704, 2003

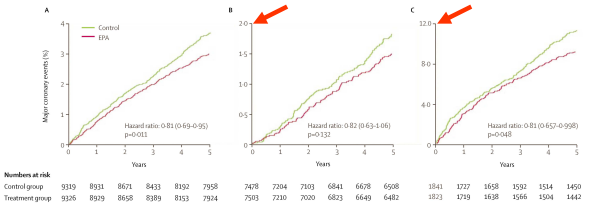
Van de Poll, Voeding Nu 2007

Fish is high in EPA and DHA

Richtlijnen Goede Voeding 2006: 450 mg/dag

JELIS study
Statin vs. Statin+1,800 mg EPA

18,645 Japanese hypercholesterolemic (≥6.5 mmol/L) patients



total study population **primary prevention** **secondary prevention**

Yokoyama, Lancet 2007

Adequaat gebied van inname voor vet(zuren) voor de volwassen bevolking

totaal vet (en%)	20-40	in energiebalans
	20-30 à 35	bij positieve energiebalans
linolzuur (en%)	2	
α-linoleenzuur (en%)	1	
(n-3) vetzuren in vis[a] (mg)	**450 mg/dag**	
cis-onverzadigde vetzuren (en%)	8-38[b]	in energiebalans
	8-28/33[b]	bij positieve energiebalans
verzadigde vetzuren (en%)	zo laag mogelijk	aanvaardbare bovengrens 10 en%
enkelvoudig trans-onverzadigde vetzuren (en%)	zo laag mogelijk	aanvaardbare bovengrens 1 en%

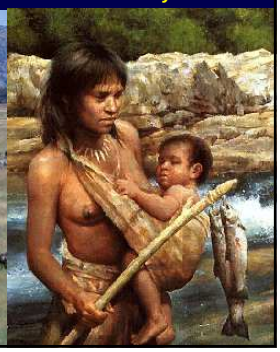
[a] visolievetzuren
[b] theoretische bovengrens

Richtlijnen Goede Voeding, 2006

Remnant needs of our land-water interface diet

Iodine
Vitamin D
Vitamin A
LCP (AA, EPA, DHA)

The savanna hypothesis is in error, we lived at the interface of water and land and ate a water-shore diet from those rich ecosystems



Fossils of our 6-2.5 Mya ancestors are mainly found at present and former interfaces of (fresh) water and land

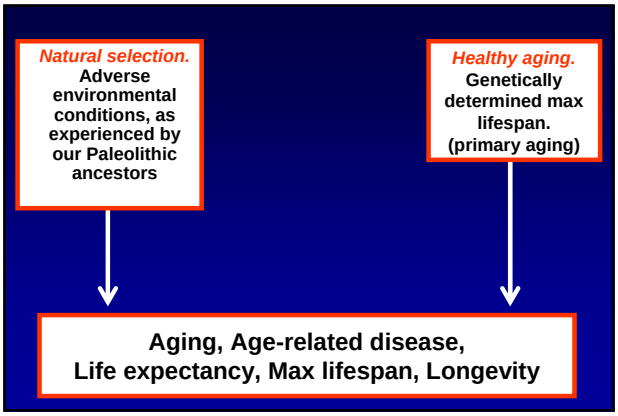
Food for brain: AA and DHA in fish available to hominids in Rift Valley Lake Nyasa (Tanzania) and Lake Turkana (Kenya)

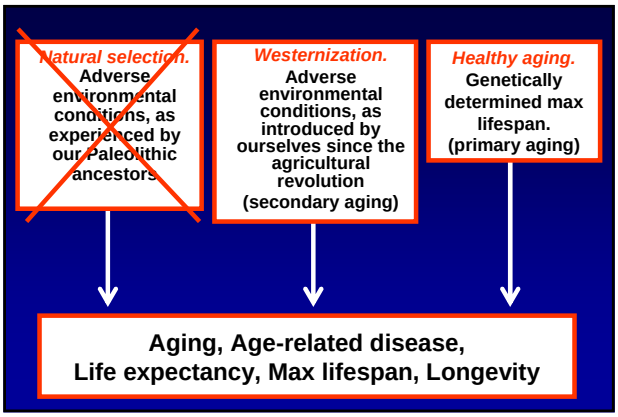
	fat	AA	DHA
	g/100 g	mg/100 g	mg/100 g
Mbelele (catfish)	10,3	421	842
Perch	2,6	190	447
Njenu (carp)	4,9	270	363
Tilapia species	2,3	184	343
Kambale (local sp)	1,8	99	227
Mfui (local sp)	1,1	84	200

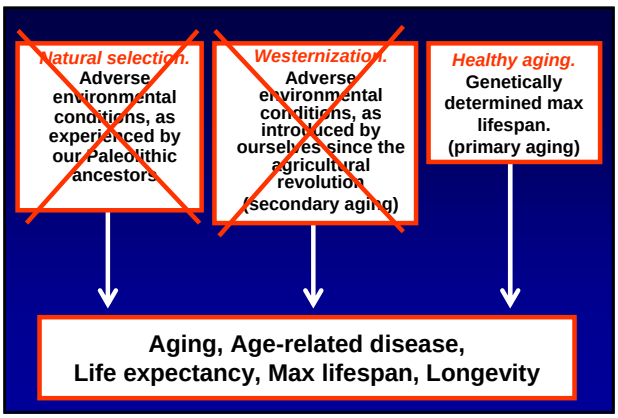
Hunter-gatherer mortality

1. Infectious disease (GI, respiratory)
2. Violence (within the species)
3. Famine

Hill, J Hum Evol 2007

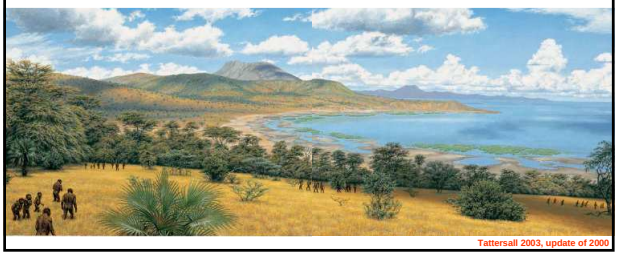

Natural selection.
Adverse environmental conditions, as experienced by our Paleolithic ancestors
Healthy aging.
Genetically determined max lifespan.
(primary aging)
Aging, Age-related disease,
Life expectancy, Max lifespan, Longevity


Natural selection.
Adverse environmental conditions, as experienced by our Paleolithic ancestors
Westernization.
Adverse environmental conditions, as introduced by ourselves since the agricultural revolution
(secondary aging)
Healthy aging.
Genetically determined max lifespan.
(primary aging)
Aging, Age-related disease,
Life expectancy, Max lifespan, Longevity


Natural selection.
Adverse environmental conditions, as experienced by our Paleolithic ancestors
Westernization.
Adverse environmental conditions, as introduced by ourselves since the agricultural revolution
(secondary aging)
Healthy aging.
Genetically determined max lifespan.
(primary aging)
Aging, Age-related disease,
Life expectancy, Max lifespan, Longevity

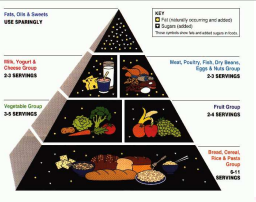
“Socially we are people of the 21st century, but genetically we remain citizens of the Paleolithic era’’

O’Keefe and Cordain, Mayo Clin Proc 2004

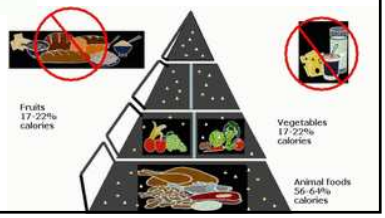


Tattersall 2003, update of 2000

Modern hunter gatherers hunt in supermarkets

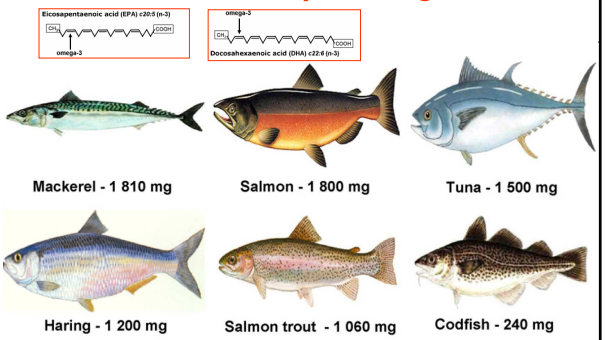


The ‘truncated’ food pyramid



What remains is fruits/vegetables and animal foods

EPA and DHA per 100 g fish



Fedacko Pathophysiology 2007

This is not okay

It is both fatness and fitness!

Healthy aging

The end