



A fascinating history of the divergence from whole foods to ultra-processed foods

*"Dis moi ce que tu manges, je te dirai ce que tu es,"*  
*"Tell me what you eat, and I will tell you what you are"*  
Brillat-Savarin, 1825

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To know where we are, we must first understand where we came from



# Darwins' vision of evolution



The organic world is a product of the operation of discoverable natural forces (evolutionary discourses), and such changes (phenotypic or genotypic) in organisms are not spastic or stochastic (Darwin, 1859).

Evolutionary adaptations occur when organisms experience modified external or environmental conditions resulting in an evolutionary discourse between the environment and its genetic profile.

Is diet capable of acting as an evolutionary discourse resulting in detectable differences among populations?

*Jean Baptiste Lamarck*  
Nature, in producing in succession every species of animal, and beginning with the least perfect or simplest to end their work with the most perfect, has gradually complicated their structure

*Robert Edmond Grant*  
Relationships of natural objects to each other, and to render more uniform and precise the language of their description, material bodies are divided into kingdoms, subkingdoms, classes, subclasses, orders, suborders, genera, subgenera, species, subspecies, varieties and subvarieties; and these terms never interchange

*Charles Robert Darwin*  
As many more individuals of each species are born than can possibly survive; and as, consequently, there is a frequently recurring struggle for existence, it follows that any being, if it vary however slightly in any manner profitable to itself, under the complex and sometimes varying conditions of life, will have a better chance of surviving, and thus be naturally selected

*Thomas Henry Huxley*  
Many more individuals of each species are born than can possibly survive; and consequently, a recurring struggle for existence, it follows that any being, if it vary however slightly in any manner profitable to itself, under the complex and sometimes varying conditions of life, will have a better chance of surviving, and naturally selected

*Sir Michael Foster*  
The body as a whole may, from a chemical point of view, be considered as a mass of various chemical substances, representing altogether a considerable capital of potential energy

*Henry Newell Martin*  
The direct influence of temperature variation upon the rate of beat of the dog's heart

*William Thompson Sedgwick*  
Father of the modern public health movement in America with a focus on sanitation and bacteriology

*Samuel Cate Prescott*  
Canned foods must be processed with a time-temperature sufficient to kill the most heat-resistant bacteria present leading to research of processing time-temperature studies

*Bernard Emerson Procter*  
Preservation of food by irradiation and formation of the International Institute of Food Technologists

*Herbert Oscar Hultin*  
Founding father of Food Biochemistry early work on enzymatic formation of volatile aromas and flavors

*David Warick Stanley*  
Correlated food microstructure to texture in food systems, including biological membranes, ice cream, and protein gelation

*Alejandro Gregor Marangoni*  
Hierarchical structures in colloidal fat crystal networks and their impact of food physical properties

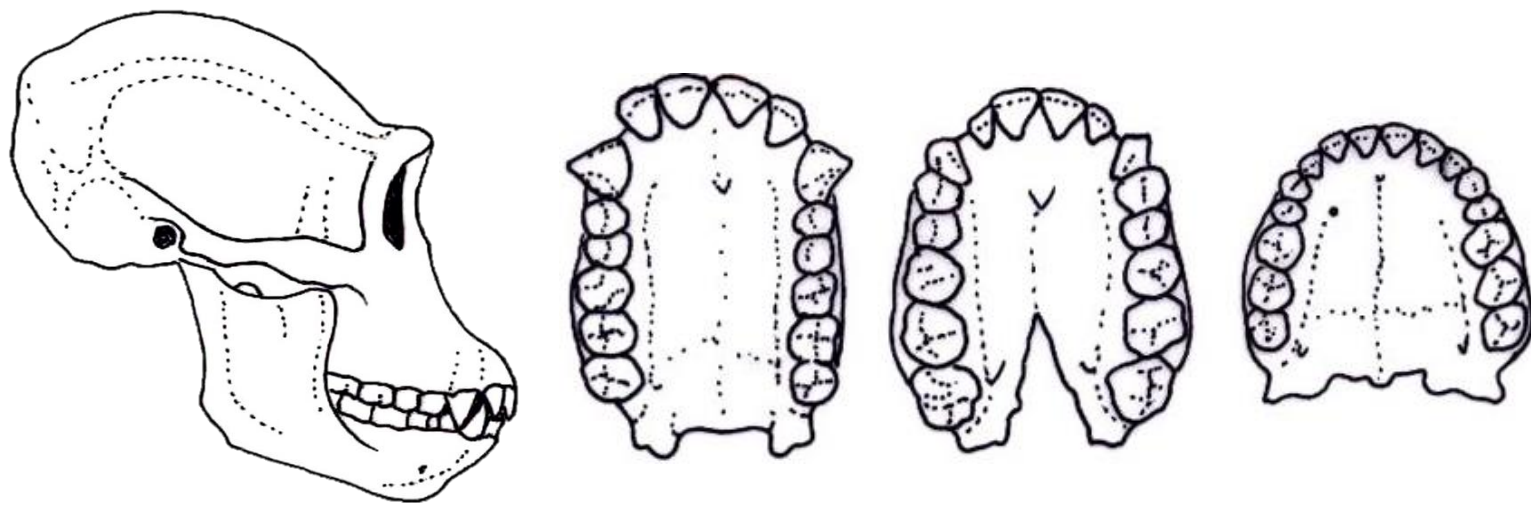
*Michael Armin Rogers*  
Molecular synthon coding of small molecules to self-assemble in dilute environments



*Ph.D. Ancestry*



# Diet and Tooth Size



- 7.0 million years ago, a diastema (gap) was next to each canine tooth to fit the larger canines when closing the jaw, and the tooth rows were and parallel rows
  - 5.5 million years ago, canines started to become smaller
  - 3.5 million years ago, teeth arranged in rows slightly wider at the back
  - 1.8 million years ago, canines became short and relatively blunt like ours
  - 250,000 years ago, our jaws became shorter, and teeth smaller arranged in a tight parabolic arc
- 
- Today there is a relationship between the foods consumed and incisor row length in a range of living anthropoids
    - Species with larger incisors consume larger, tougher fruits
    - Smaller front teeth feed on smaller foods, or those that require less extensive incisal preparation, such as leaves or berries

PNAS Proceedings of the National Academy of Sciences of the United States of America

Keyword, Author, or DOI

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NEW RESEARCH IN Physical Sciences Social Sciences

**Diet and the evolution of the earliest human ancestors**

Mark F. Teaford and Peter S. Ungar

PNAS December 5, 2000. 97 (25) 13506-13511; <https://doi.org/10.1073/pnas.260368897>

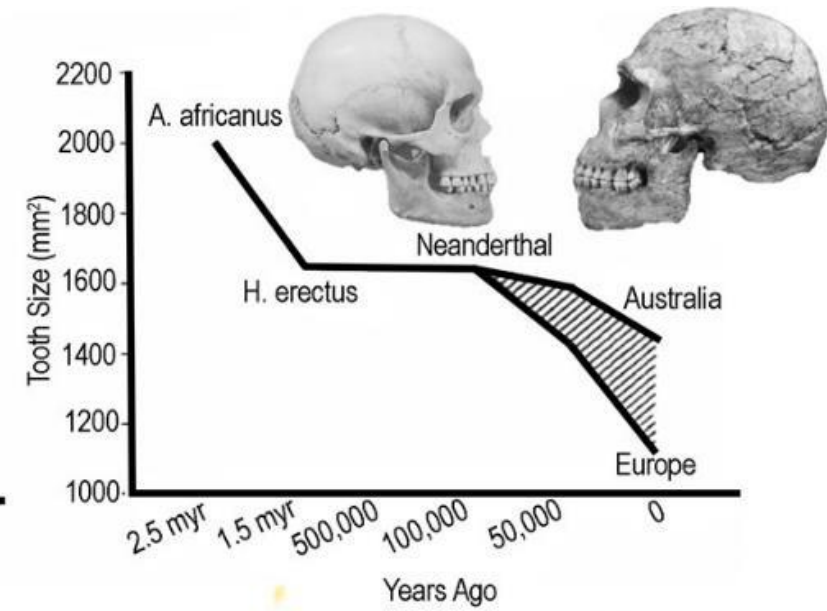
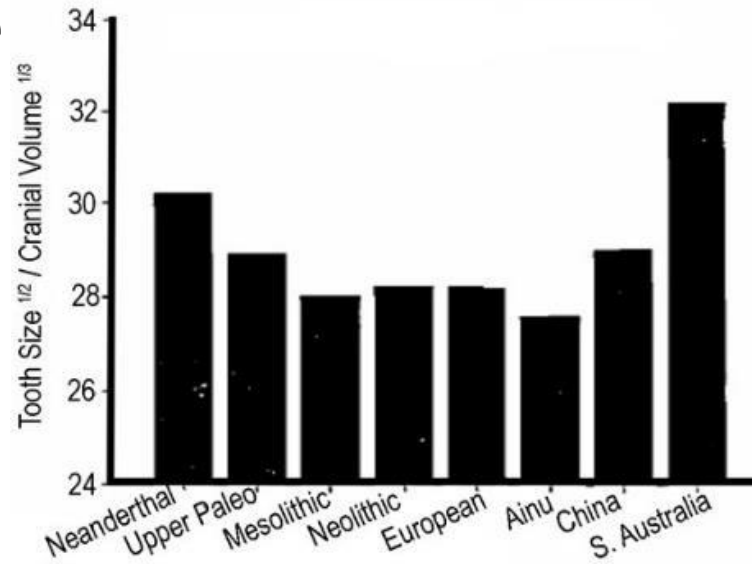
# Diet and Tooth Size

## Advances in Dental Anthropology

4  
What Big Teeth You Had Grandma!  
Human Tooth Size, Past and Present

C. Loring Brace, Shelley L. Smith, and Kevin D. Hunt

Museum of Anthropology, University Museum Building, Ann Arbor, Michigan 48109 (C.L.B.); Center for Human Growth and Development, University of Michigan, Ann Arbor, Michigan 48109 (S.L.S.); Department of Anthropology, Peabody Museum, Harvard University, Cambridge, Massachusetts 02138 (K.D.H.)



Tooth sizes (dentation) changed dramatically during the late Pleistocene in the Northern Hemisphere and differences in tooth size are still observed today based on which Hemisphere your family lineage resided!

The principal function of dentition has always remained the processing of foods; contrary to the expectation that diet should be the focus of our concern, “the important thing to look to is not so much the foods itself but what was done to it before it was eaten.”

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# What if there was scientific evidence?

## Advances in **Dental Anthropology**

4

What Big Teeth You Had Grandma!  
Human Tooth Size, Past and Present

C. Loring Brace, Shelley L. Smith, and Kevin D. Hunt 1991, PAGES 33-57

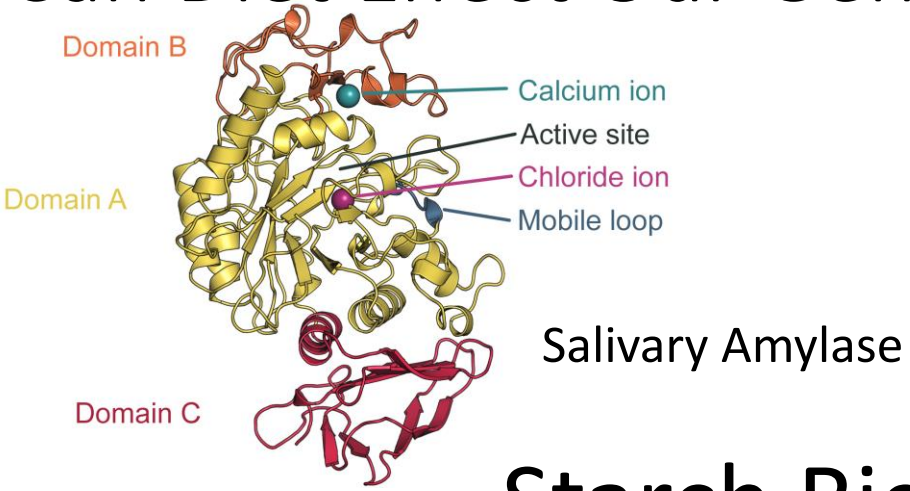
Museum of Anthropology, University Museums Building, Ann Arbor, Michigan 48109 (C.L.B.); Center for Human Growth and Development, University of Michigan, Ann Arbor, Michigan 48109 (S.L.S.); Department of Anthropology, Peabody Museum, Harvard University, Cambridge, Massachusetts 02138 (K.D.H.)

- It is clear that relative tooth sizes (dentation) changed dramatically in the Northern Hemisphere during the late Pleistocene (ice age - 2.5 million to 11,700 years ago)
- The authors state that there are differences in tooth size still observable today based on which Hemisphere your family tree resides!

So what happened, why did they change?

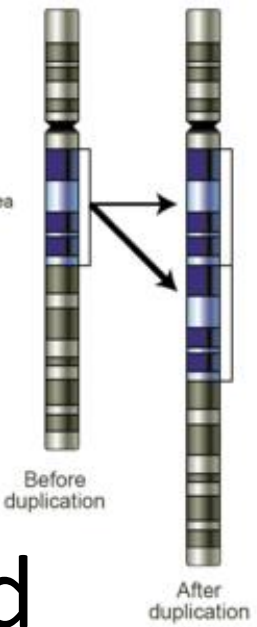


# Can Diet Effect Our Genes? A look at isolated million-year-old diets



AMY-1 gene codes salivary amylase

AMY-1 gene copy number from 2 to < 10



## Starch Rich

## Diet

## Starch Devoid

Hadza hunter-gatherers



Baobab Fruit

Yakut coldwater fish

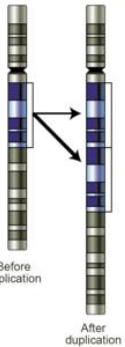




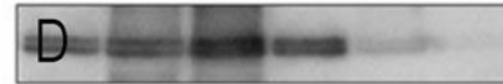
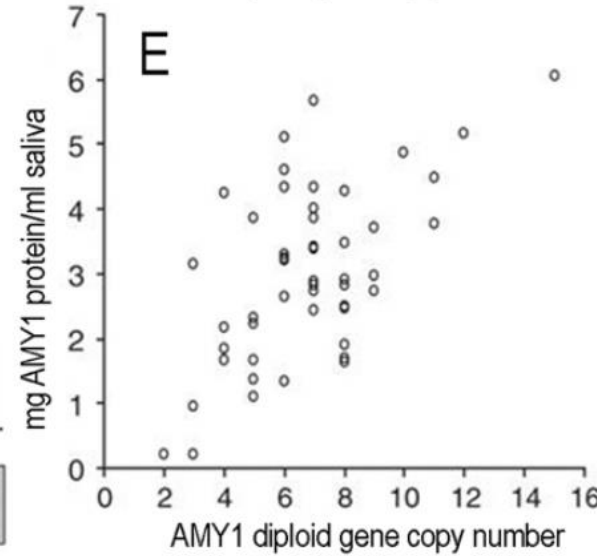
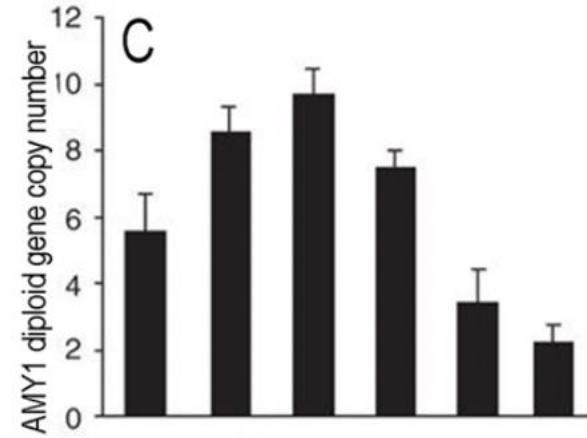
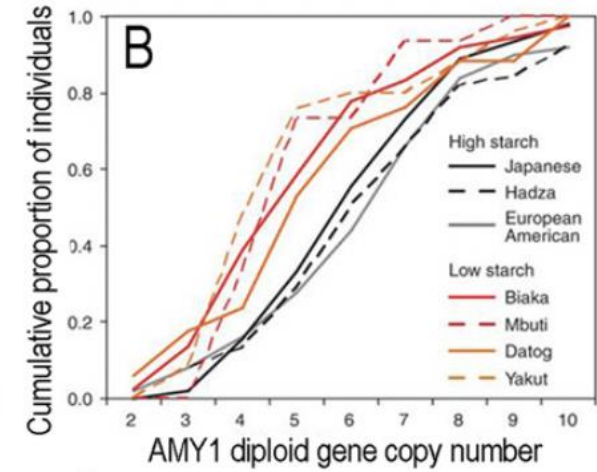
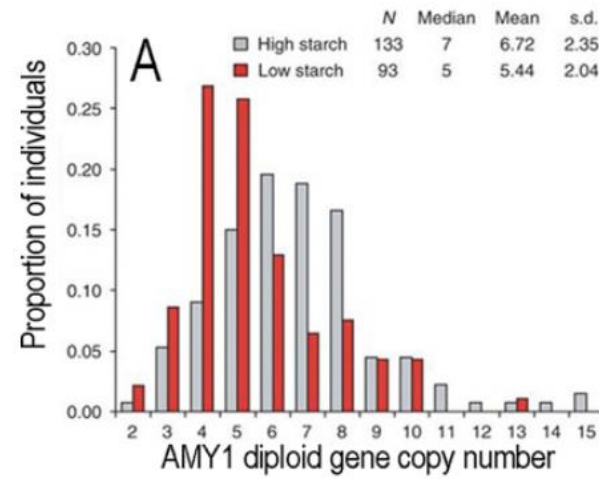
# DOES OUR DIET DRIVE EVOLUTION?

A FASCINATING LOOK AT OUR HISTORY

- 1) **High-starch consuming populations:** Japanese, European American and Hadza hunter-gatherers (rely extensively on starch-rich roots and tubers)
- 2) **Low-starch consuming populations:** rainforest hunter-gatherers (e.g. **Biaka and Mbuti**), pastoralists (e.g. **Datog**) and a pastoralist, fishing society (e.g. **Yakut**)



- Populations that consume low-starch diets have lower AMY-1 gene copy number than populations that consume high-starch diets which have greater AMY-1 gene duplication and higher diploid gene copy numbers
- Populations with higher AMY-1 gene copy numbers produce more salivary amylase (a digestive enzyme for starch)



Letter | Published: 09 September 2007

## Diet and the evolution of human amylase gene copy number variation

George H Perry, Nathaniel J Dominy, Katrina G Claw, Arthur S Lee, Heike Fiegler, Richard Redon, John Werner, Fernando A Villanea, Joanna L Mountain, Rajeev Misra, Nigel P Carter, Charles Lee & Anne C Stone

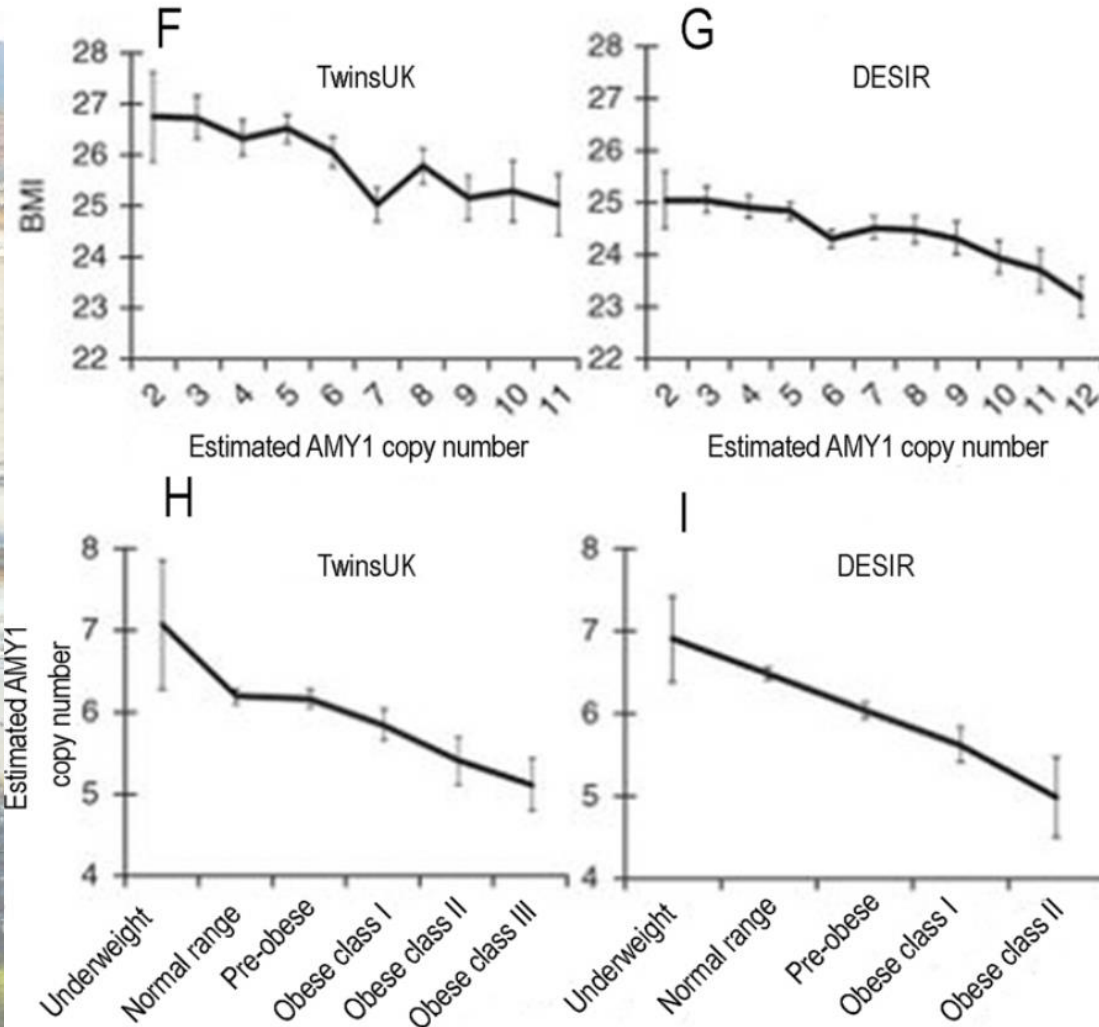
Nature Genetics 39, 1256–1260 (2007) | Download Citation



# DOES OUR DIET DRIVE EVOLUTION?

A FASCINATING LOOK AT OUR HISTORY

- A 1.19 difference in AMY1 copy number translates to an 8-fold difference in risk of obesity between the individuals who's copy number > 9) compared to those with a copy number < 4
- High-starch diets have positive selection forces driving higher AMY1 gene copy numbers leading to higher salivary amylase protein concentration



**Changing diet = Changing genome!  
Predisposition to obesity?!?**



Letter | Published: 30 March 2014

## Low copy number of the salivary amylase gene predisposes to obesity

Mario Falchi, Julia Sarah El-Sayed Moustafa [...] Philippe Froguel

Nature Genetics 46, 492–497 (2014) | [Download Citation](#)



# Other Genetic Differences Taste Genetics

RESEARCH

Open Access

Prevalence of cilantro (*Coriandrum sativum*)  
disliking among different ethnocultural groups

Lilli Mauer<sup>1</sup> and Ahmed El-Sohehy<sup>2\*</sup>

**Disliking cilantro based on ethnocultural groups**

21% East & 7% South Asian, 17% Caucasians, 14% African, 4% Hispanics, & 3% Middle Eastern

**Genetic component** to cilantro taste suggests that cilantro dislike stems from a genetic variant in the olfactory receptors OR6A2 gene.

**Single polymorphic mutation** in the OR6A2 olfactory receptor genes makes cilantro taste soapy.


 **BMC** Part of Springer Nature

 **Flavour**

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Research | [Open access](#) | Published: 29 November 2012

**A genetic variant near olfactory receptor genes  
influences cilantro preference**

[Nicholas Eriksson](#) , [Shirley Wu](#), [Chuong B Do](#), [Amy K Kiefer](#), [Joyce Y Tung](#), [Joanna L Mountain](#), [David A Hinds](#) & [Uta Francke](#)

*Flavour* **1**, Article number: 22 (2012) | [Cite this article](#)



Coriander

Cilantro



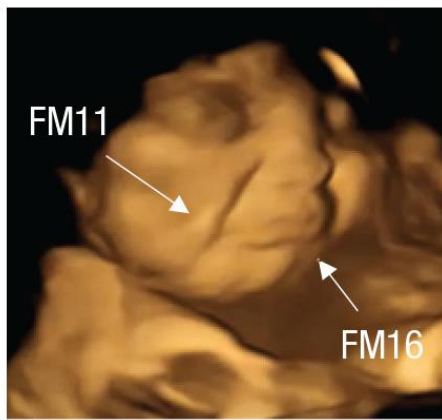




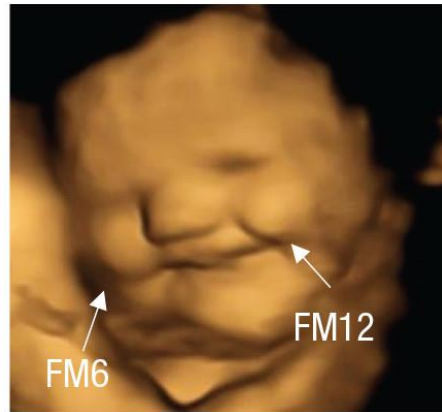
Research Article

# Flavor Sensing in Utero and Emerging Discriminative Behaviors in the Human Fetus

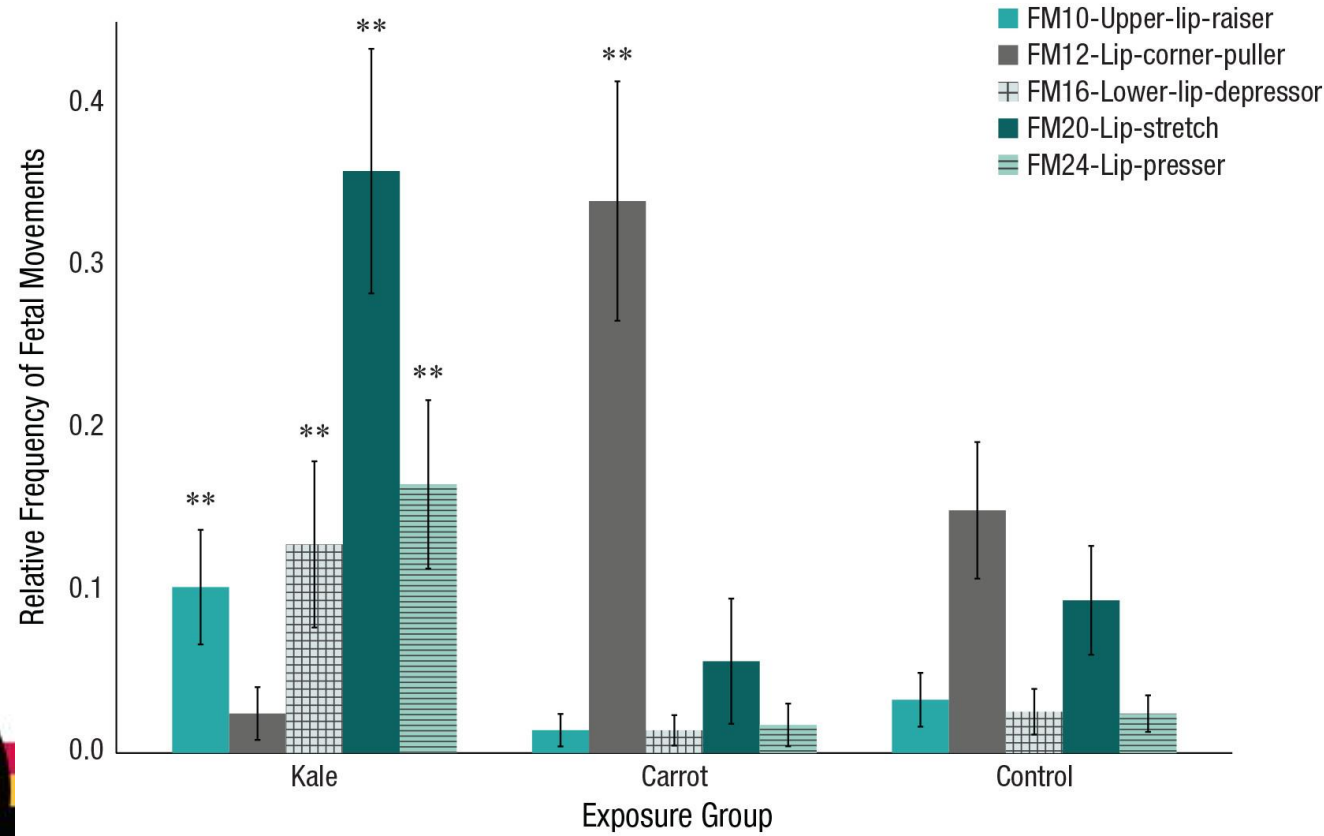
Beyza Ustun <sup>1</sup>, Nadja Reissland <sup>1</sup>, Judith Covey<sup>1</sup>, Benoist Schaal<sup>2</sup>, and Jacqueline Blissett<sup>3</sup>



Example of cry-face of a kale-exposed fetus



Laughter-face of a carrot-exposed fetus









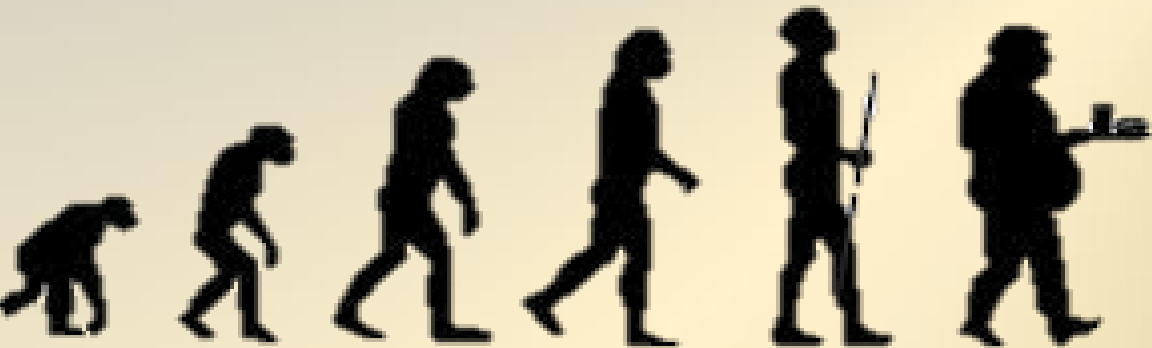
# Food For Thought

- Western countries single largest cause of morbidity and mortality are diet-related chronic diseases!!!!
- 50-65% of the western adult population are afflicted with a diet related disease.
- Food related disease do not stem from a single element of food consumption, but rather from a complex interaction of multiple nutritional factors.



# Food for Thought

For the first time in human history, non-communicable diseases (i.e., cancer, diabetes mellitus, cardiovascular diseases), all of which are related, in part, to diet, are responsible for a larger percentage (46.8 %) of the mortality rate than communicable disease (41.0 %)

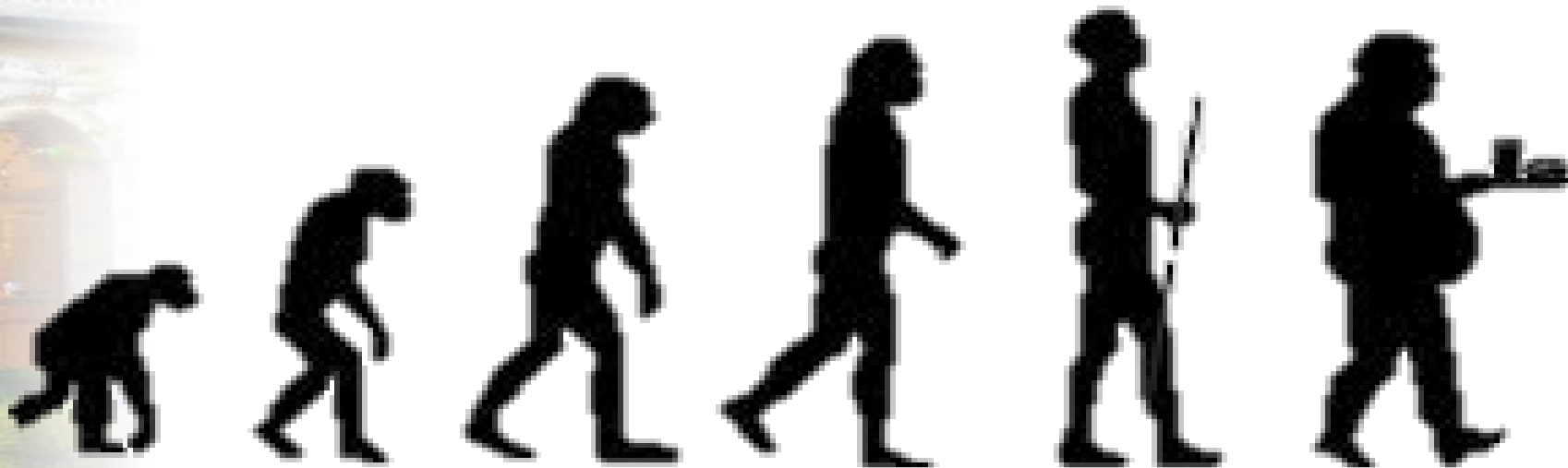




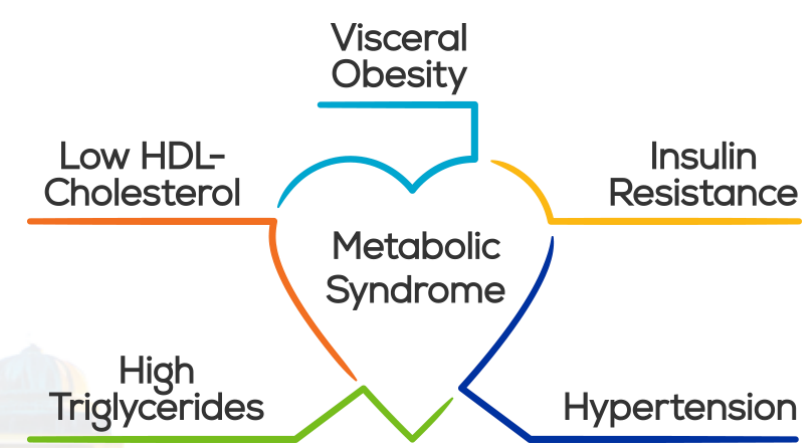
# Food for Thought

Global health leaders have even shifted attention from germs to what United Nations Secretary-General Ban Ki-Moon calls “a public health emergency in slow motion”.

Perhaps, what is even more shocking is that **non-communicable diseases are responsible for nearly 2/3<sup>rds</sup> of deaths in the Americas.**

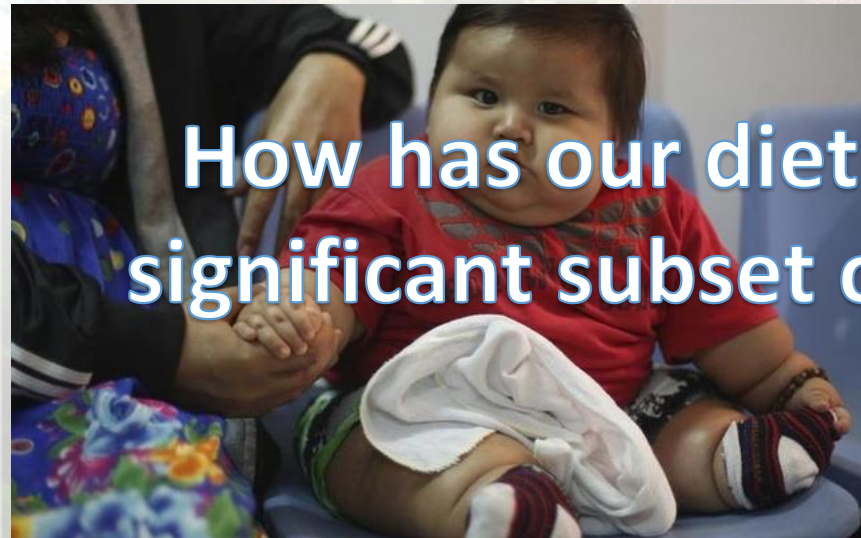


# Food As we Knew it



- Diets today have led to the development of an **entirely new form of malnutrition**, unheard of less than a century ago
- Countless populations have at least double digit percentages of people with metabolic syndrome (MetS);
  - Obesity is fundamental to MetS, as it precedes the emergence of impaired insulin sensitivity, dyslipidaemia, hypertension and a 1.6-fold increase in mortality

How has our diet changed, so drastically, as to lead to a significant subset of the global population diagnosed with MetS?







Food and Agriculture Organization  
of the United Nations

FAO recognized a disturbing trend of “displacement of dietary patterns based on meals and dishes prepared from unprocessed or minimally processed foods by those that are increasingly based on ultra-processed food”

# PRE-INDUSTRIAL REVOLUTION FOOD ENVIRONMENT



# TODAY'S Food Environment





# Food As we Knew It



~5% Sweet corn



45% corn silage



## Isolation & Purification



FORMULATION



45% - Ultra Processed Foods





NOVA Classification of Foods				
	Group 1	Group 2	Group 3	Group 4
	Unprocessed or minimally processed foods	Processed culinary ingredients	Processed foods	Ultra-processed foods
Level of Processing	Low	Medium	Medium/High	High
Types of Food	Edible parts of plants (seeds, fruits, leaves, stems, roots), or of animals (muscle, eggs, milk), and also fungi, algae and water.	Ingredients used to make stews, soups and broths, salads, breads, preserves, drinks and desserts.	Bottled vegetables, canned fish, fruits in syrup, cheeses and freshly made breads.	Soft drinks, sweet or savory snacks, reconstituted meats and pre-prepared frozen dishes (i.e., formulations made primary from substances derived from foods and additives, with limited intact foods.
Unit Operations	drying, crushing, grinding, fractioning, filtering, roasting, boiling, non-alcoholic fermentation, pasteurization, refrigeration, chilling, freezing, placing in containers and vacuum-packaging.	Pressing, refining, grinding, milling and drying.	Preservation or cooking methods, and, in the case of breads and cheese, non-alcoholic fermentation.	Hydrogenation and hydrolyzation, extrusion and molding, and pre-processing for frying (i.e., a multitude of sequences of processes used to combine many ingredients and to create product.
Outcome of Processing	Preserve natural foods, to make them suitable for storage, or to make them safe or edible or more pleasant to consume	Durable products suitable for use in home and restaurant kitchens to prepare, season and cook Group 1 foods.	Recognizable as modified versions of Group 1 foods with increase the durability, or to modify or enhance their sensory qualities.	Branded, convenient (durable, ready to consume), hyper-palatable and profitable (low-cost ingredients) food products.
Location of Processing	Significant home or in restaurant kitchen preparation.	Industrially processed ingredients to be used with significant home or in restaurant kitchen preparation.	Predominately industrially processed.	Industrially processed with minimal processed at household level.



Norman Borlaug  
Nobel Prize 1970

# The man who fed the world

## Forgotten Benefactor of Humanity

by GREGG EASTERBROOK

*Norman Borlaug,  
the agronomist whose discoveries  
sparked the Green Revolution, has saved literally  
millions of lives, yet he is hardly  
a household name*

“The form of agriculture that Borlaug preaches may have prevented a billion deaths”





# The man who fed the world

**Shuttle Breeding:** Used Mexico's two growing seasons  
Would breed wheat in the central highlands  
Then immediately plant the seeds in the northern lowlands  
The difference in altitudes and temperatures would allow more crops to be grown each year

Disproved that seeds needed a rest period after harvesting

Norman Borlaug  
Nobel Prize 1970



Norman Borlaug  
Nobel Prize 1970

# The man who fed the world

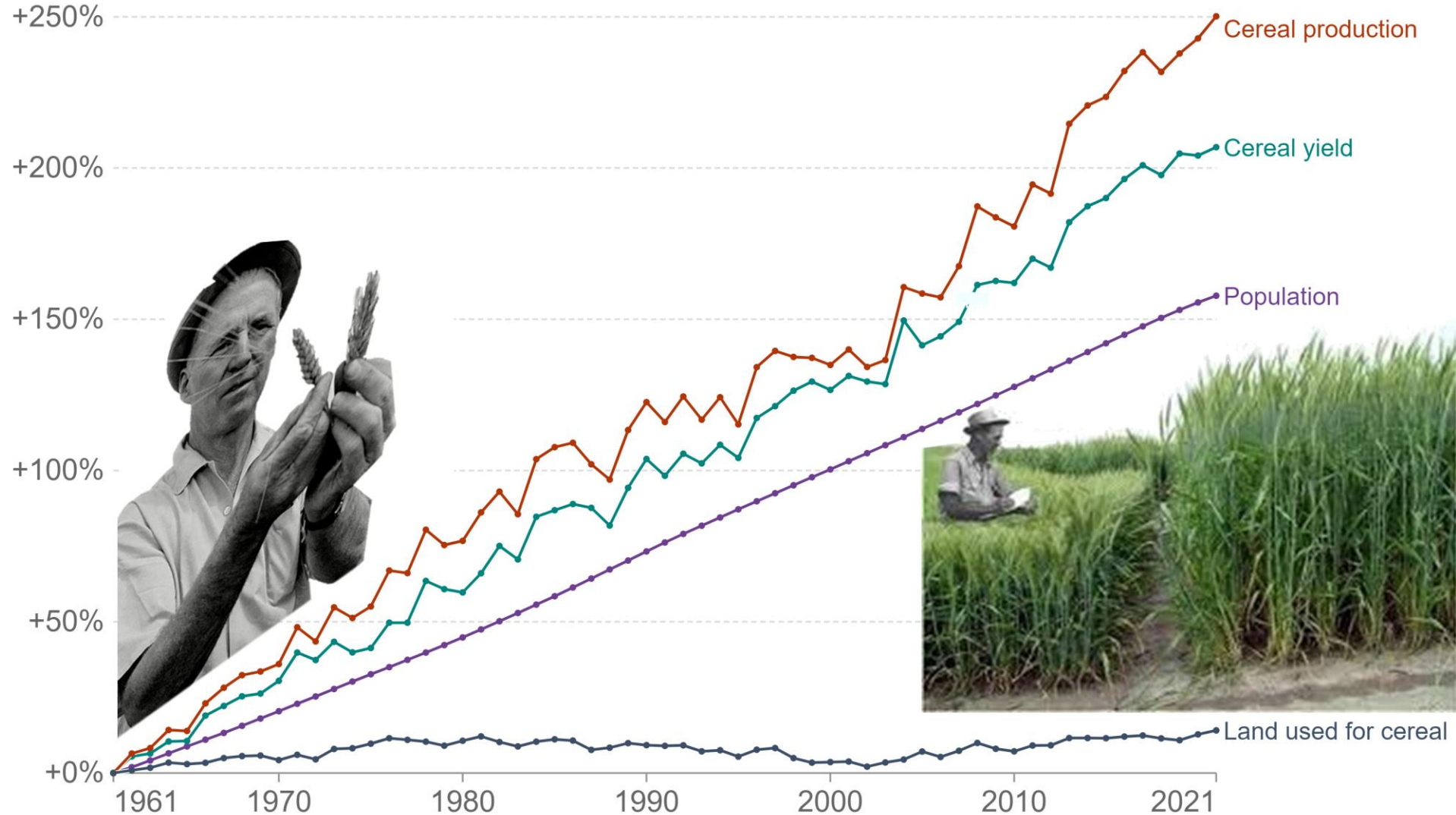
- Developed semi-dwarf, disease-resistant wheat varieties
- Within 3 years 95% of Mexico's wheat crops used the semi-dwarf varieties developed by Borlaug
- That year, the harvest was six times larger
- Mexico became self-sufficient and a net exporter of wheat





# Change in cereal production, yield, land use and population, World

All figures are indexed to the start year of the timeline. This means the first year of the time-series is given the value zero.



Source: Our World in Data based on World Bank; Food and Agriculture Organization of the United Nations  
OurWorldInData.org/crop-yields • CC BY

# What Changed?

- 70% of our daily energy intake was unavailable prior to the industrial revolution
  - Refined sugar
  - Refined vegetable oil
  - Cereals
  - Dairy products (limited)
  - Alcohol (limited)
  - Mixed foods
    - Cookies, pizza, soft drinks, ice cream...etc!!!!

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 **Origins and evolution of the Western diet: health implications for the 21st century** FREE

Loren Cordain ✉, S Boyd Eaton, Anthony Sebastian, Neil Mann, Staffan Lindeberg, Bruce A Watkins, James H O'Keefe, Janette Brand-Miller

*The American Journal of Clinical Nutrition*, Volume 81, Issue 2, 1 February 2005, Pages 341-354, <https://doi.org/10.1093/ajcn.81.2.341>

Volume 81, Issue 2



## Refined Oils

Consumption increase 1909 to 1999  
130% increase in salad & cooking oils  
140% increase in shortening  
410% increase in margarine

## Crystalline Sugar

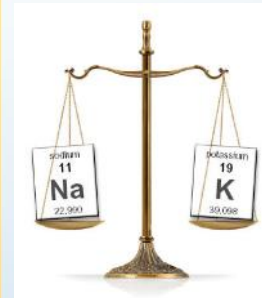
Preindustrial revolution <1kg per capita  
Post industrial revolution 6.8kg per capita  
Currently 69kg per capita



## Salt

Preindustrial revolution diets had more potassium than sodium

Per capita Na intake 2760 milligrams (mg)  
Allowable Intake (AI) Na: 1500 mg/day  
Upper limit (UL) Na: 2300 mg/day  
Allowable Intake (AI) K: 4.5 g/day  
Upper limit (UL) K: NA



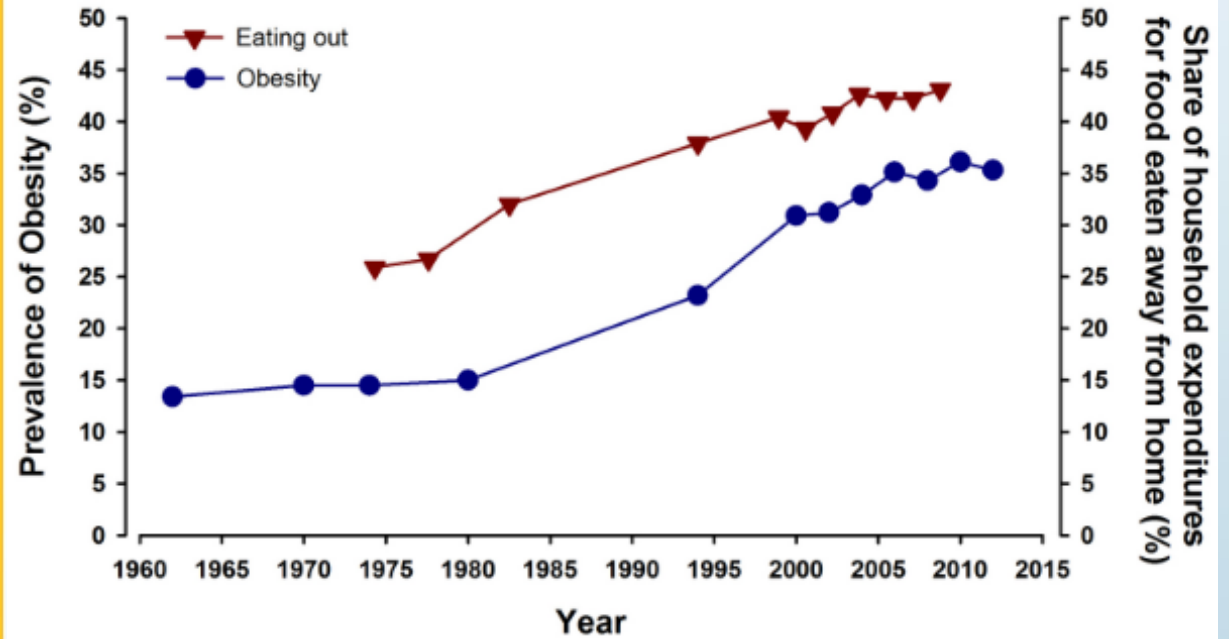
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Food eaten away from home and obesity prevalence have both risen steadily since 1970



# DEATH OF THE HOME COOKED MEALS

# Ultra-processed foods and Health

- Individuals in the highest quintile of UFP consumption had significantly higher body-mass-index (0.94 kg/m<sup>2</sup>; 95% CI: 0.42,1.47) and higher odds of being obese (OR = 1.98; 95% CI: 1.26,3.12) and excess weight (OR = 1.26; 95% CI: 0.95,1.69) compared with those in the lowest quintile of UFP consumption (Louzada, et al., 2015).
- Diets high (>74.2 % calories from UFPs) was associated with 1.61 units higher BMI (95 % CI 1.11, 2.10), 4.07 cm greater waist circumference (95 % CI 2.94, 5.19) and 48, 53 and 62 % higher odds of BMI≥25 kg/m<sup>2</sup>, BMI≥30 kg/m<sup>2</sup> and abdominal obesity (Juil & Hemmingsson, 2015)
- Numerous large cohort studies have shown diets high in UFPs concur with higher incidence of non-communicable diseases

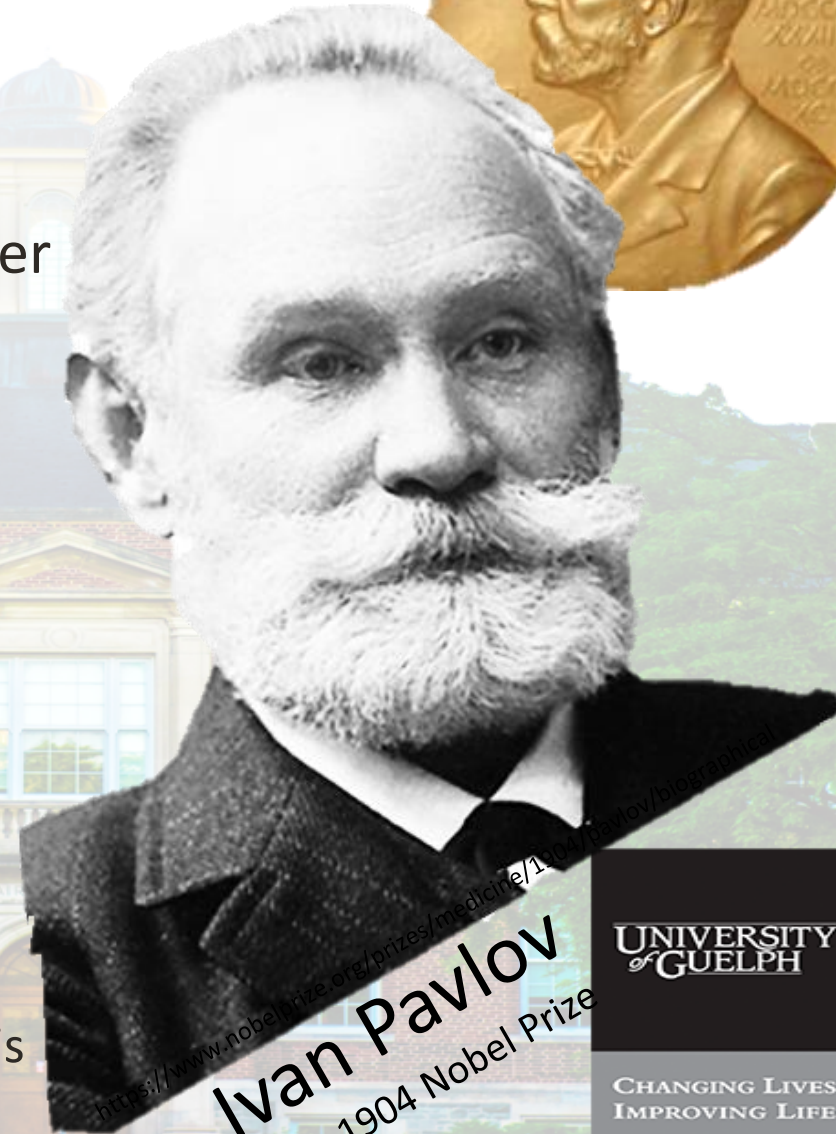
Canadians on average get ~48% of their calories from UPF



# Is Our Understanding of Human Nutrition Complete?

- First studies to understand human nutrition and Founder of Physiology of Digestion
- Developed surgical use of fistulas to study functions of various organs under relatively normal conditions

“With extreme clarity he showed that the nervous system played the dominant part in regulating the digestive process, and this discovery is in fact the basis of modern physiology of digestion”



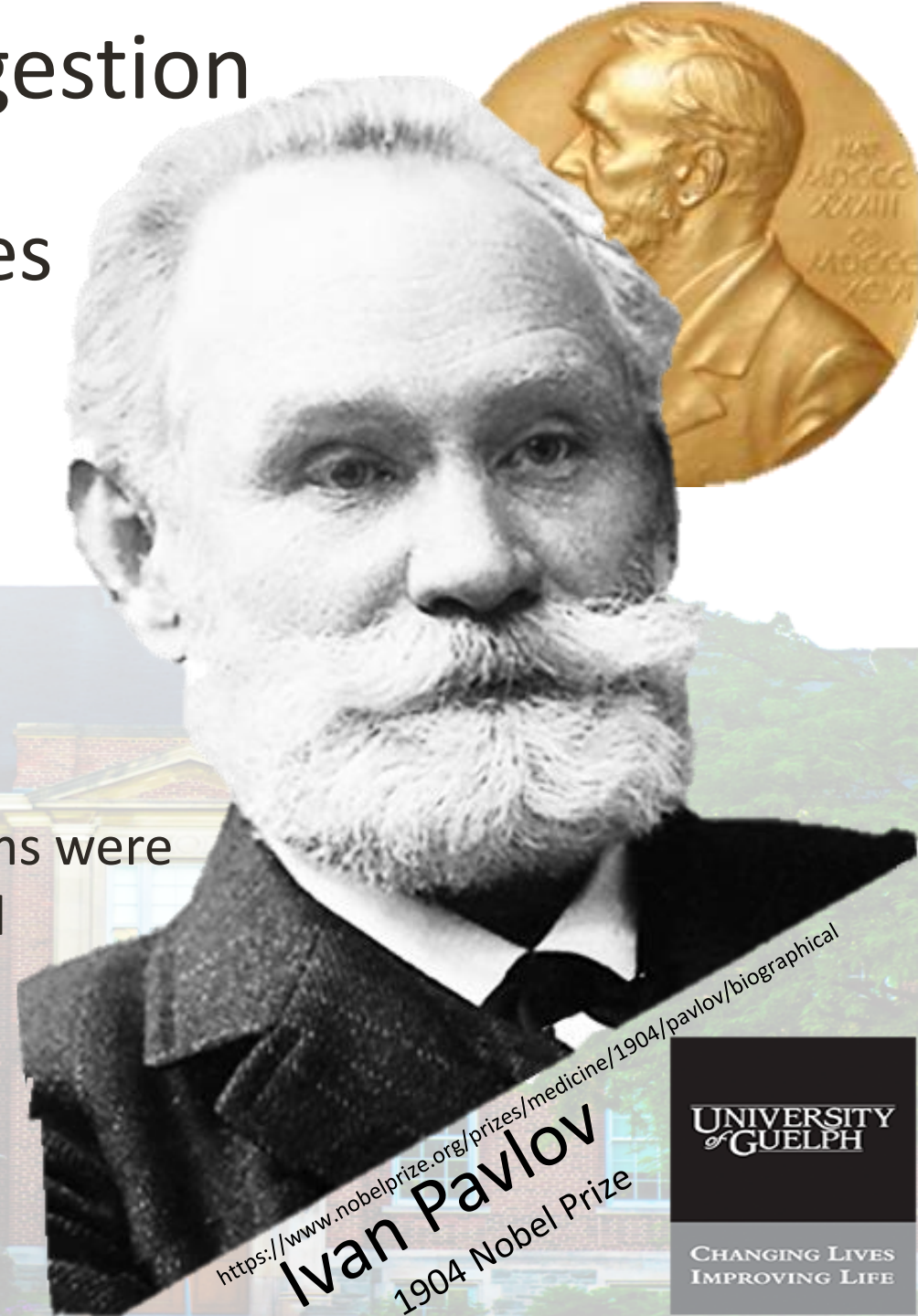


# Founder of Physiology of Digestion

- Science of conditioned reflexes

Pavlov rejected Sechenov's 'psychic' salivary secretion hypothesis and proposed instead it was of a reflex nature— not permanent but temporary or a conditioned one – was involved.

Discovered that reflex mechanisms were not of psychic activity but instead experimentally proven theory of conditioned reflexes.



<https://www.nobelprize.org/prizes/medicine/1904/pavlov/biographical>  
**Ivan Pavlov**  
1904 Nobel Prize

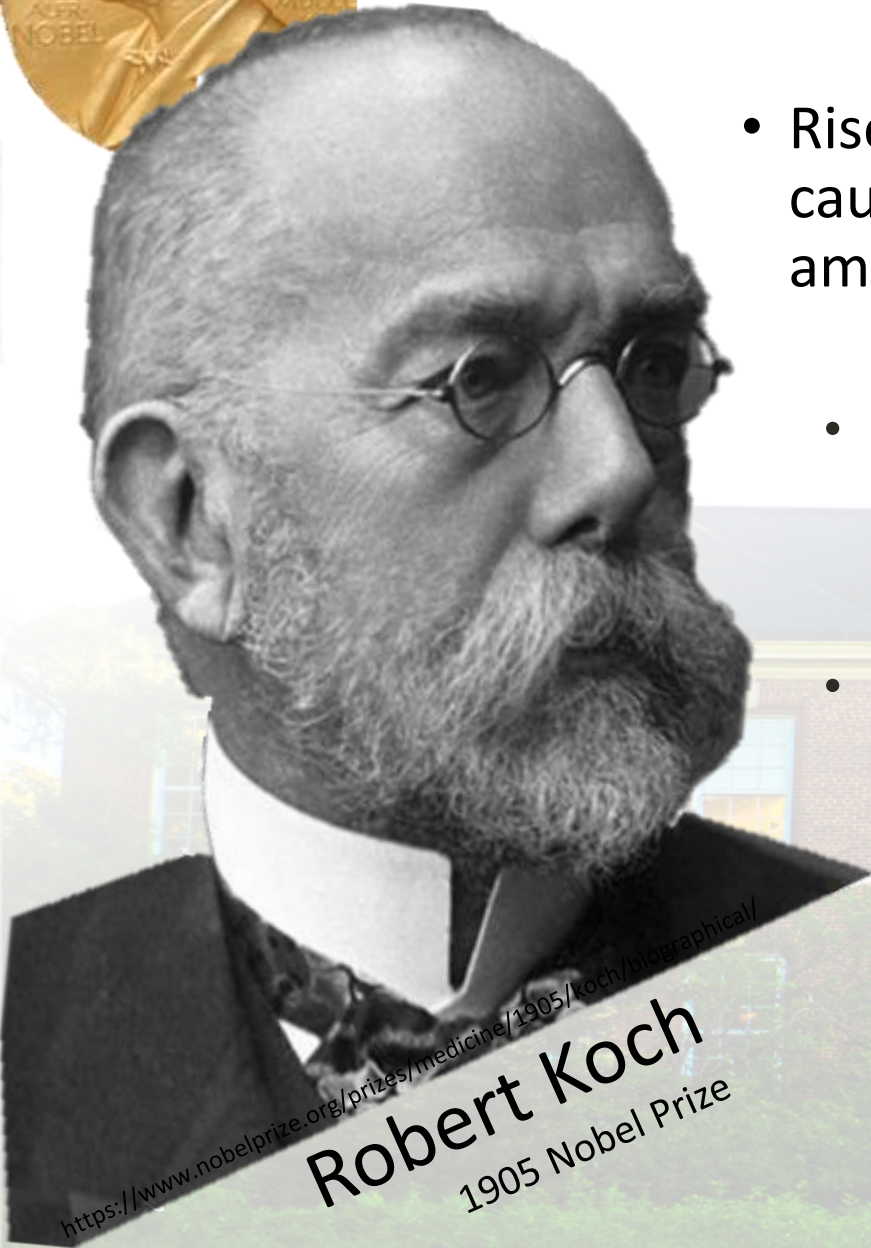
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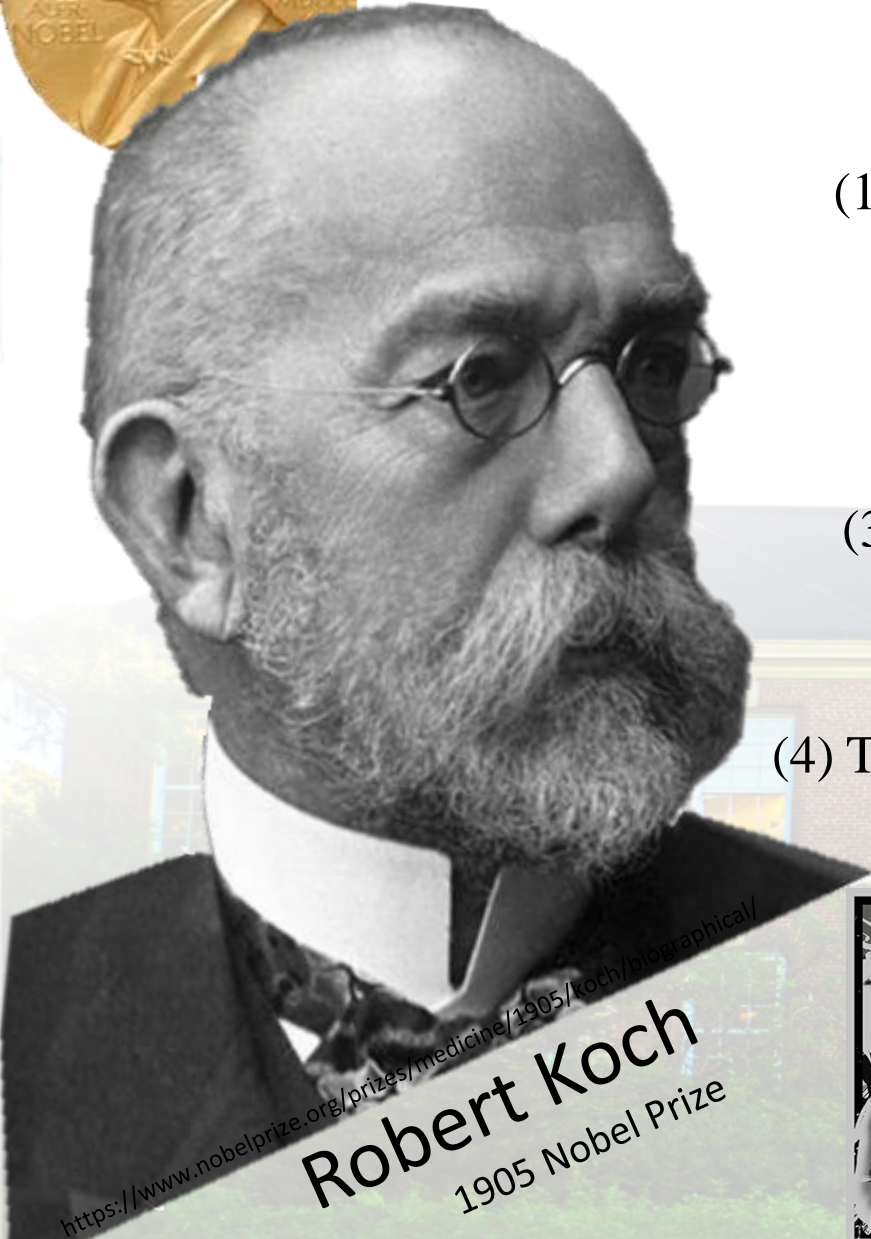
# Father of Modern Microbiology

- Rise to fame, 1876 essay on the causative agent of anthrax prevalent among farm animals, was bacillus
  - First showed bacilli when conditions are unfavorable, produce inside themselves rounded spores that resists adverse conditions, especially lack of oxygen.
  - When suitable conditions of life are restored, the spores give rise to bacilli again.
- Bacilli grown for several generations in pure cultures with no contact to any kind of animal, caused anthrax upon exposure



<https://www.nobelprize.org/prizes/medicine/1905/koch/biographical/>  
**Robert Koch**  
1905 Nobel Prize





# Koch Postulate's Four Criteria

(1) The microorganism must be found in diseased but not healthy individuals;

(2) The microorganism must be cultured from the diseased individual;

(3) Inoculation of a healthy individual with the cultured microorganism must recapitulated the disease;

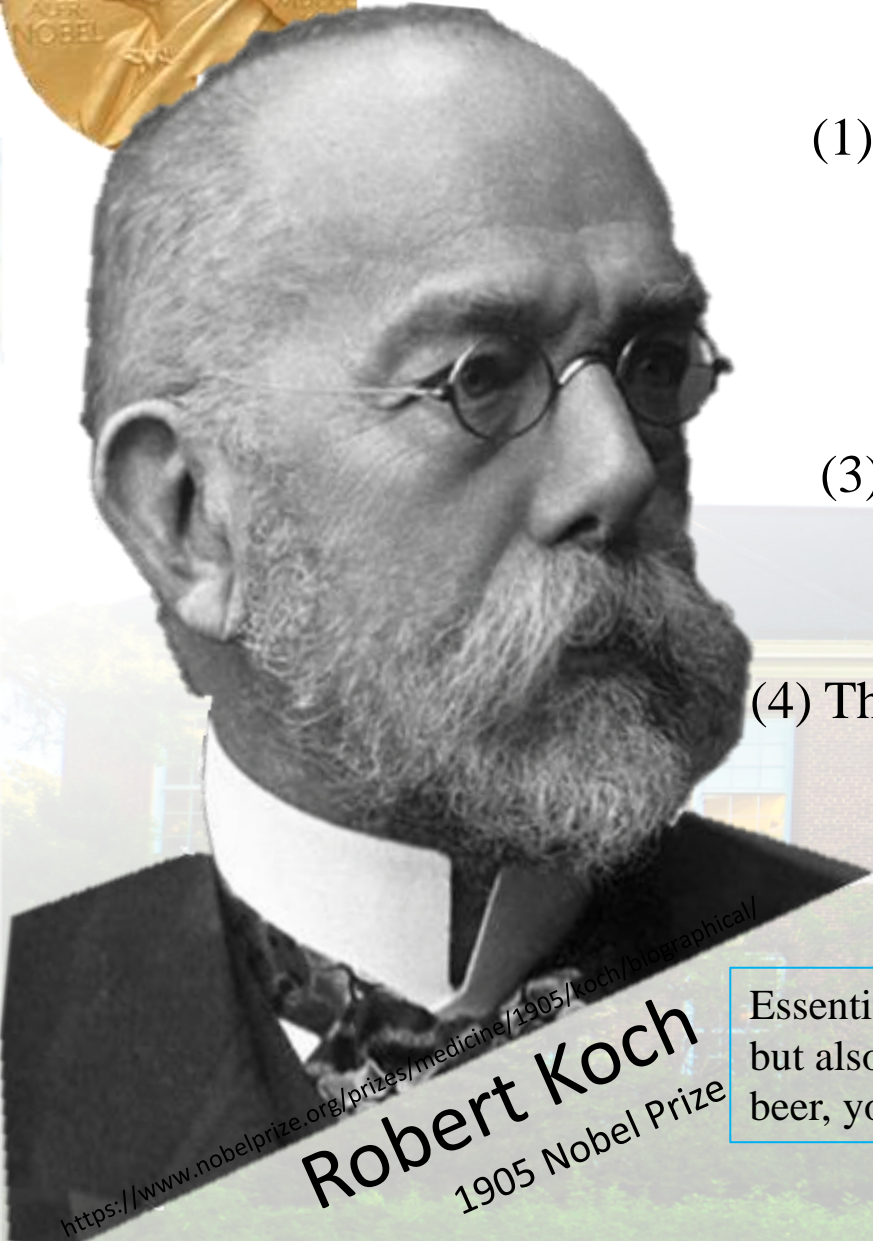
(4) The microorganism must be re-isolated from the inoculated, diseased individual and matched to the original microorganism.



**Robert Koch**  
1905 Nobel Prize

<https://www.nobelprize.org/prizes/medicine/1905/koch/biographical/>





**Robert Koch**  
1905 Nobel Prize

Essential for first food safety, but also fermentation (wine, beer, yoghurt and cheese).

Established aseptic techniques flame sterilization, tube transfer, streak plates, spread plates and pour plates methods for enumerating microorganisms.

## Koch Postulate's Four Criteria

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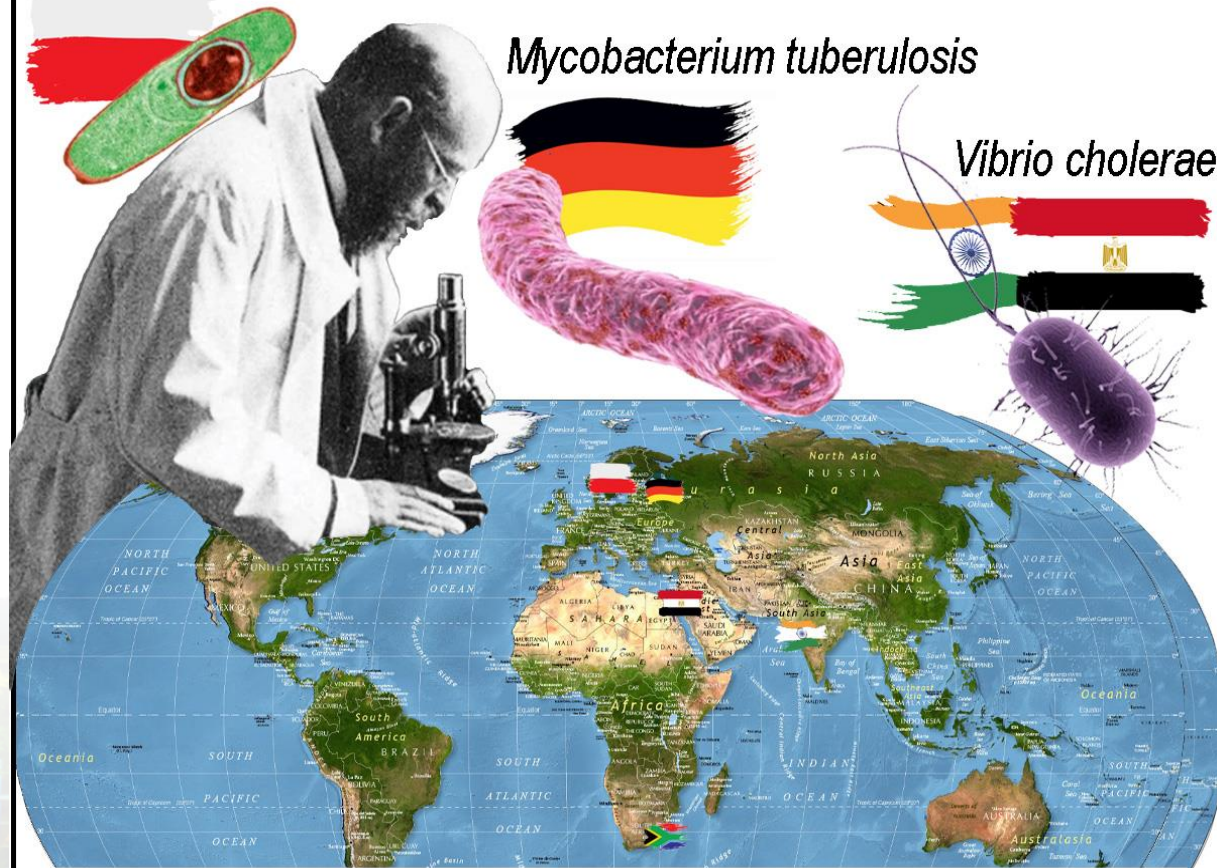


# Koch's Postulate Identified

*Bacillus anthracis*

*Mycobacterium tuberculosis*

*Vibrio cholerae*



# Robert Koch

Identified bacteria causing anthrax, cholera, & tuberculosis.

## Gin and Tonic

Tonic water, from *Cinchona bark*, contains quinine, an anti-malarial alkaloid

~1825 British officers began to mix gin with their daily ration of quinine tonic

Where Cause not Identified  
Implemented Sanitation Measures

  
Rinderpest  
(Cattle Plague)

  
Malaria  
(Control With Quinine)

  
Surra of Cattle  
&  
Plague



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# At the Same Time

## Koch's Postulate Identified

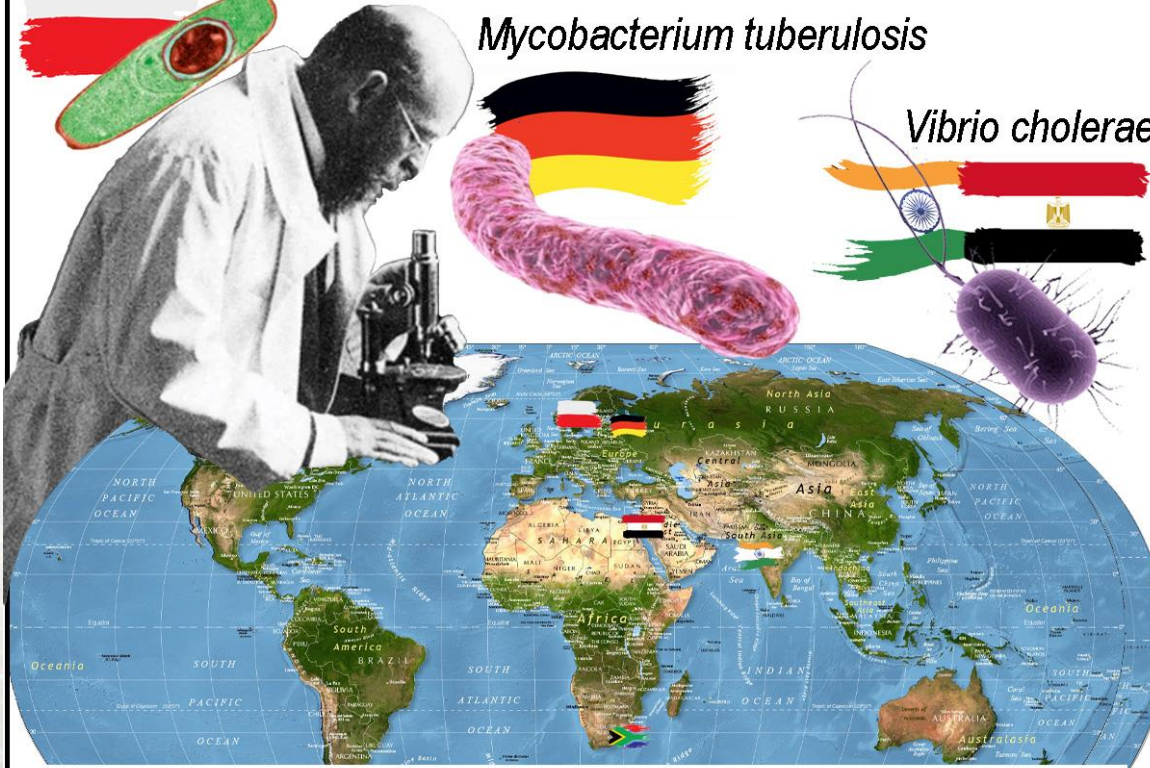
*Bacillus anthracis*



*Mycobacterium tuberculosis*



*Vibrio cholerae*



Where Cause not Identified  
Implemented Sanitation Measures



Eijkman



1875: Military Medical School of the University of Amsterdam  
 1883: Doctoral degree "Polarization of the Nerves"  
 1883: Health Officer for Java & W. Sumatra  
 1885: Returns to Holland on sick leave with Malaria  
 1885: Goes to Berlin University to study bacteriology with Koch  
 1900: Seconded Back to Dutch Indies (Pekelharig-Winkler Mission)



## Disease Characteristics

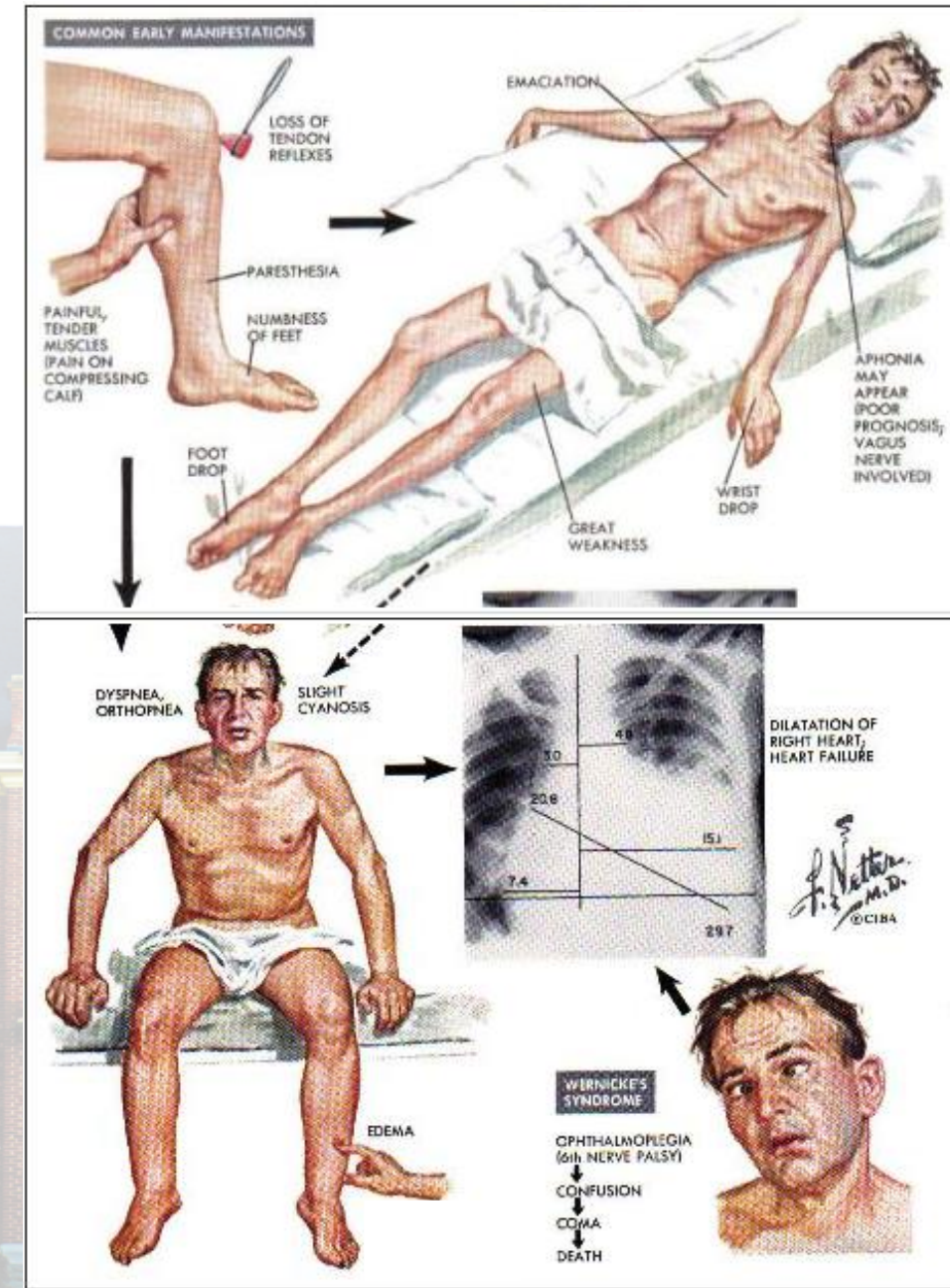
Not associated with a fever  
 Legs begin to weaken  
 Chest/Heart pounding  
 Asphyxia and death



# 1880's a Plague emerged

## Characterized by:

- By impairment of the nerves and heart
- Confusion and loss of mental acuity
  - 1) degeneration of long nerves starting in the arms and legs with atrophy of muscles and loss of reflexes
- or
  - 2) Edema resulting from cardiac failure
- If a mother was sick it would lead to heart failure of infants



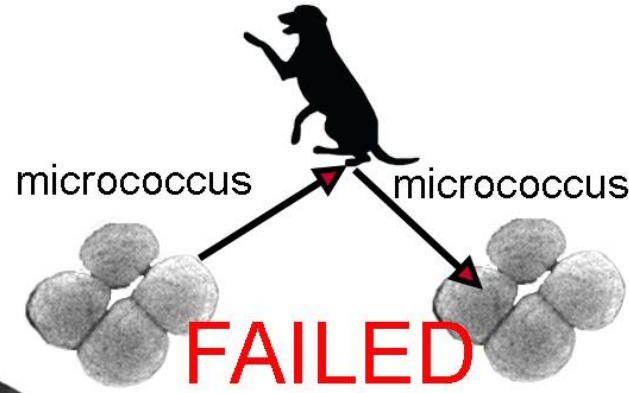


8 months later Pekelharing leaves Eijkman behind and wrote afterwards "that a micrococcus that they had isolated in the affected area was almost certainly the cause of the disease"

Pekelharing

Eijkman

## Koch's Postulate



Dutch East Indies

## Who Were at Risk?

certain classes of men  
women in the final stage of pregnancy

## Most Susceptible

Students away from home  
The warrior class  
Newly enlisted military

## Rare Among

Nobility with high incomes  
Poor porters/rickshaw drivers  
Natives living traditional lifestyles in villages





# Switches to Chickens

Control birds developed leg weakness despite being out of range of possible cross-infection

Eijkman



## Limb weakness

It was not bacteria



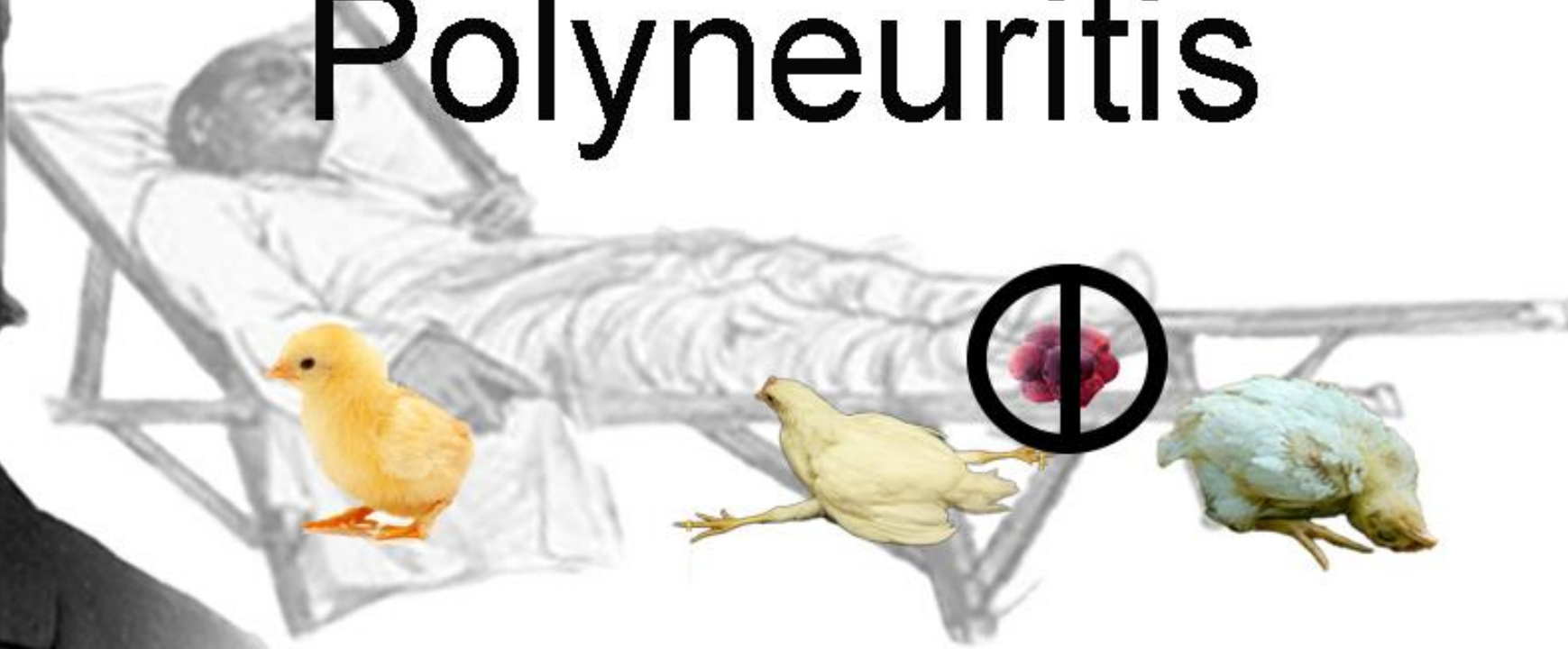
Polyneuritis





# Limb weakness Polyneuritis

Eijkman



Asked the chicken handler  
if anything changed?

# Eijkman's Nobel Finding



Cooking previous milled and 'polished' 'white' rice was sufficient to produce leg weakness, and brown (unpolished, rice (with the 'silverskin' or bran still adhering)) was not – **something in the polishings cured "Beri-beri"**.

## Amazing Fact

He also found that microbial death was logarithmic—remember why this is so important.

The Nobel Prize in Physiology or Medicine 1  
Christiaan Eijkman, Sir Frederick Hopkins

Share this: 10

### Christiaan Eijkman: Biographical



Christiaan Eijkman was born in 1858, at Nijkerk in Gelderland, the seventh child of Christiaan and Johanna, headmaster of a local school and a schoolmistress.

A year later, in 1859, he moved to Zaandam, where his father became head of a newly founded elementary school. Christiaan and his brother received a good education. In 1875, after passing his examinations, Eijkman became a student at the Medical University of Amsterdam, where he was trained as a physician in the Netherlands Indies Army, passing through all his examinations.

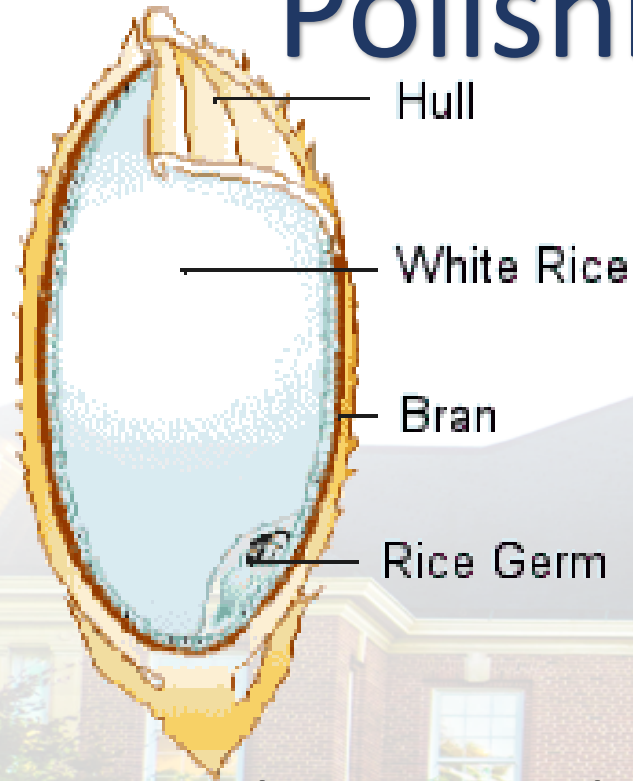


One change had been noted



# Historical Perspective of Beriberi

## Polishing and Milling




> 80% thiamine in bran



<http://www.gutenberg.org/files/14613/14613-h/14613-h.htm>

to improve its shelf life by removing layers that contain fats that can become rancid as well as to change its appearance from brown to white which often improves its acceptability by consumers. Within the bran layer are enzymes known as lipases that break down the oils in the whole grain rice.

# Our Understanding of Vitamins

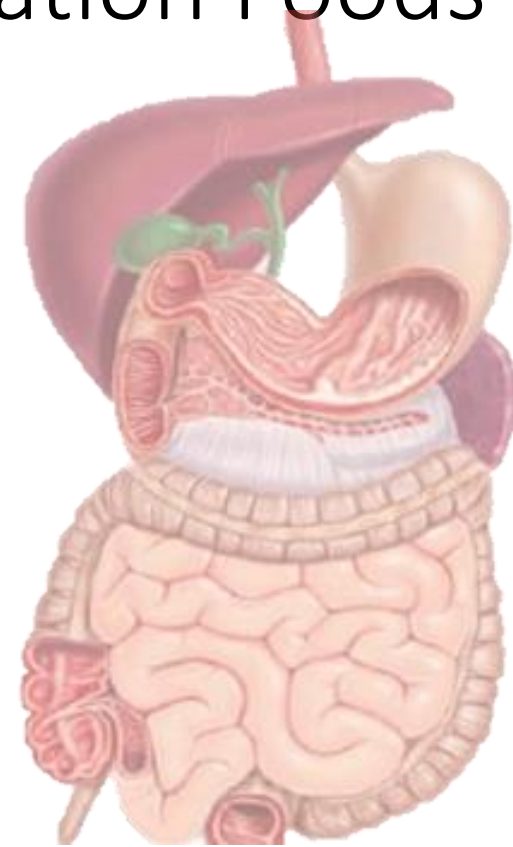
						 	 	 	 	 			 	 
Grijns 1901	Funk 1912	McCollum 1915	Mellanby 1919	Goldberger 1920	Evans 1922	Hopkins 1929	Minot 1934	Murphy 1934	Dam 1943	Szent-Gyorgyi 1937	Gyorgy 1934	Elvehjem 1937	Doisy 1943	Hodgkin 1955
beri-beri was a nutritional deficiency	Coined term Vitamin	Water soluble and fat soluble vitamin	Rickets caused by fat soluble nutrient deficiency	Pellagra caused by diet deficiency	Vitamin E	Vitamin theory 	Raw liver prevented pernicious anemia  	Vitamin K 	Vitamin C 	Vitamin B-6	Niacin prevents pellagra	Synthesized Vitamin K 	Structure of B-12 	



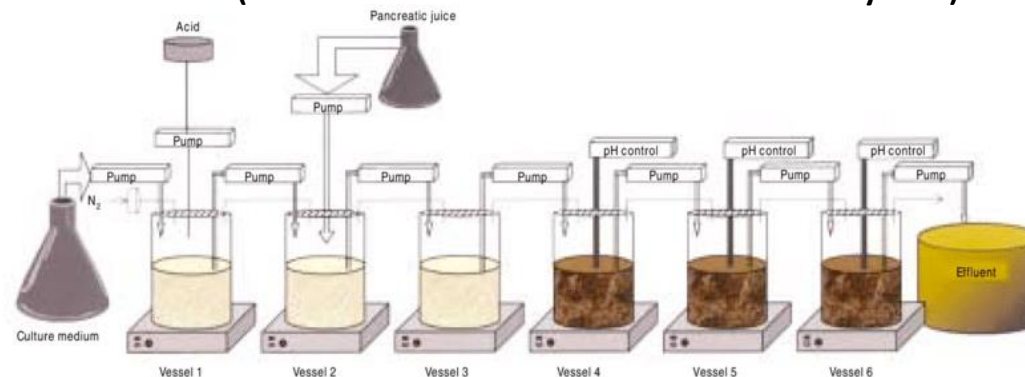
# Beyond Composition – The Next Generation Foods

## Digestion - Kinetics - Bioaccessibility

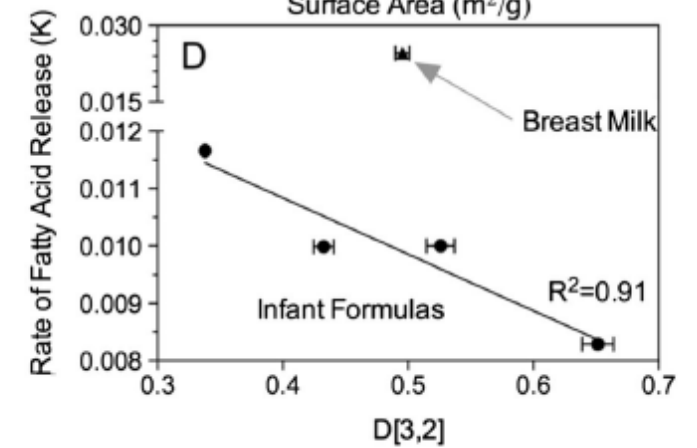
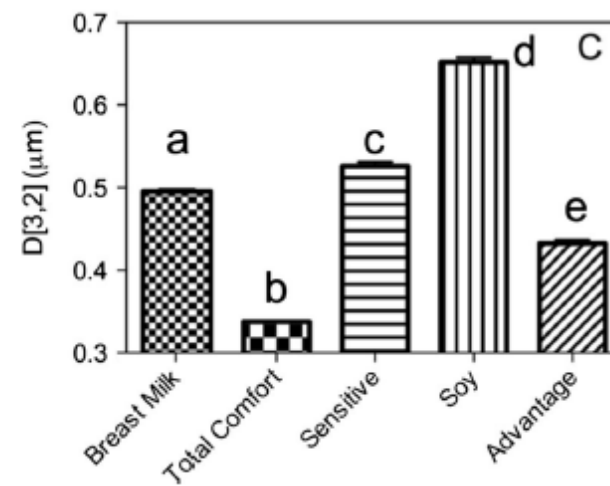
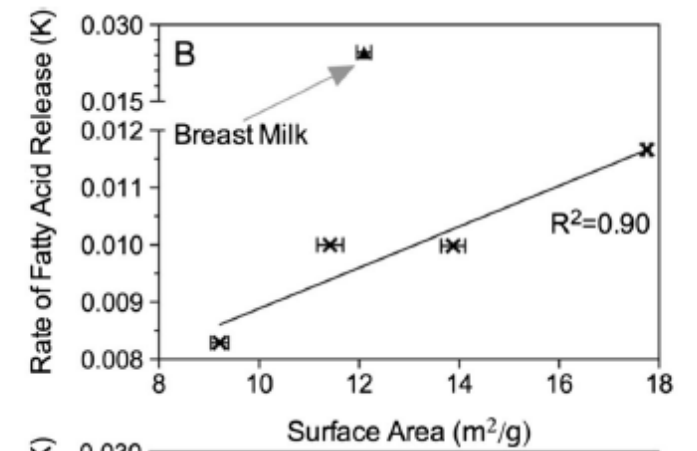
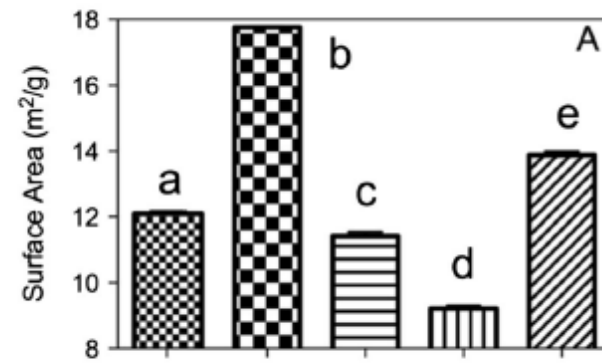
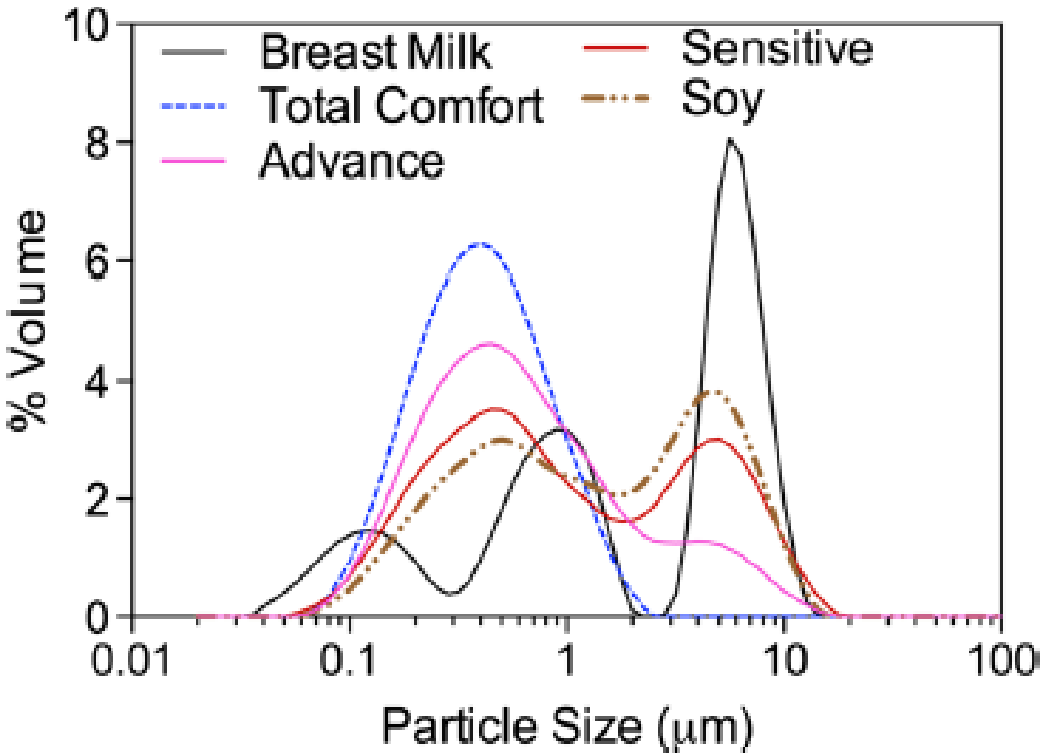
- Dynamically simulates **ALL** luminal conditions of a healthy adult
- Mimics body temperature, peristalsis, while dynamically regulating gastric emptying and transit time, pH (dynamically in the stomach & maintained in the intestinal segments), enzyme and bile secretions, and digitate filtration (mock absorption)
- The rate molecules are released from the food into the luminal fluid (bioaccessibility) are measure
- Bioaccessibility, or the release of the bioactive from the food, is often the rate limiting step



**Twin-SHIME (Simulated Human Intestinal Microbial Ecosystem)**



# Where it all started



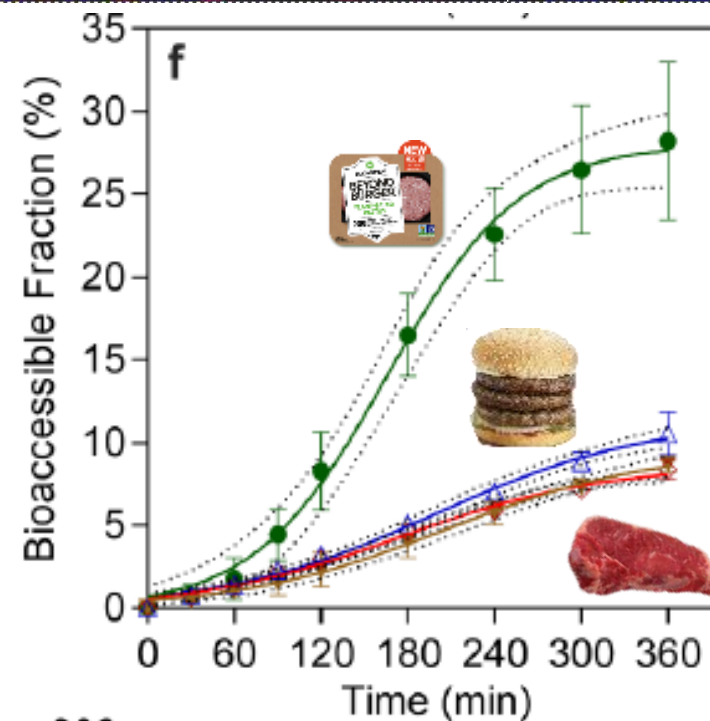
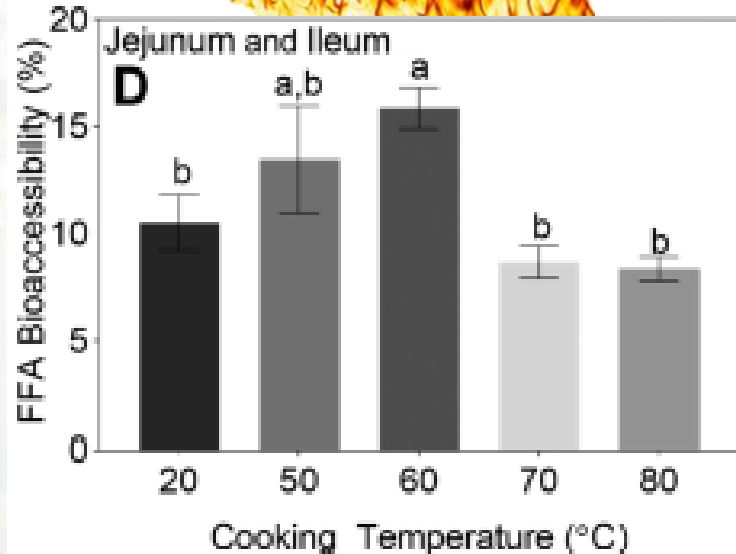
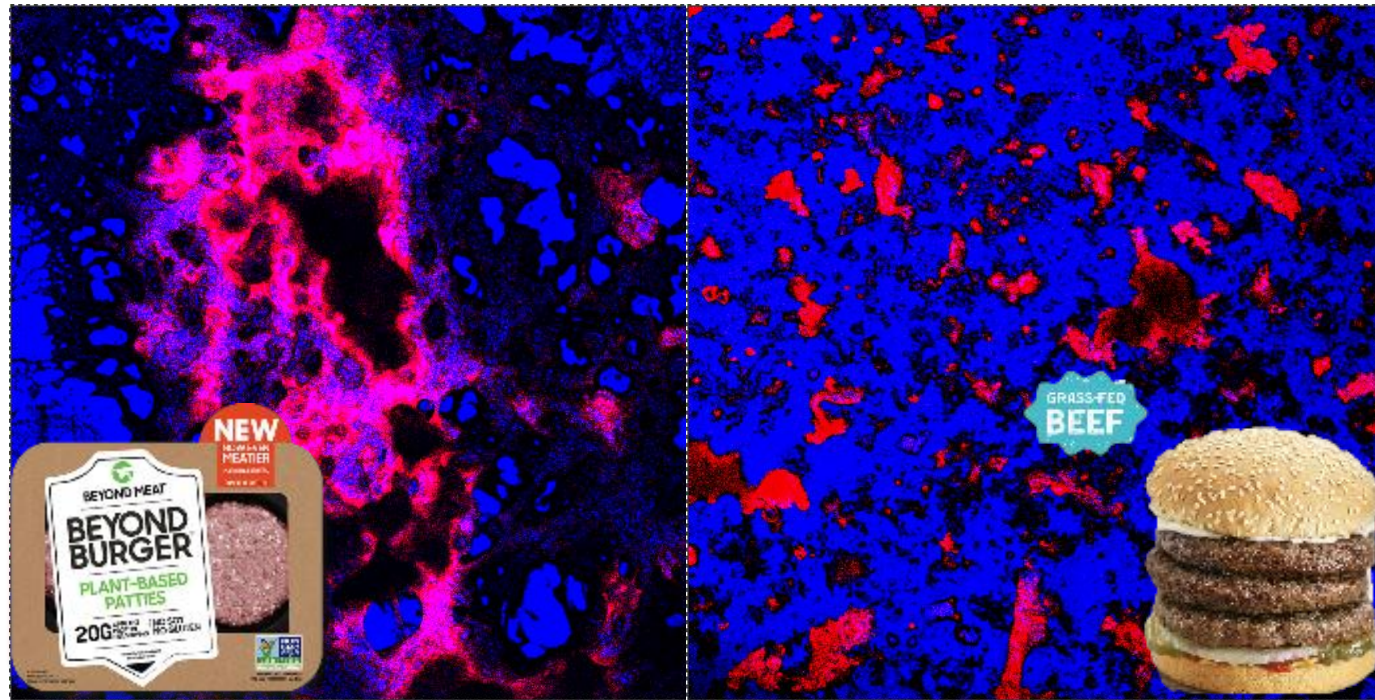
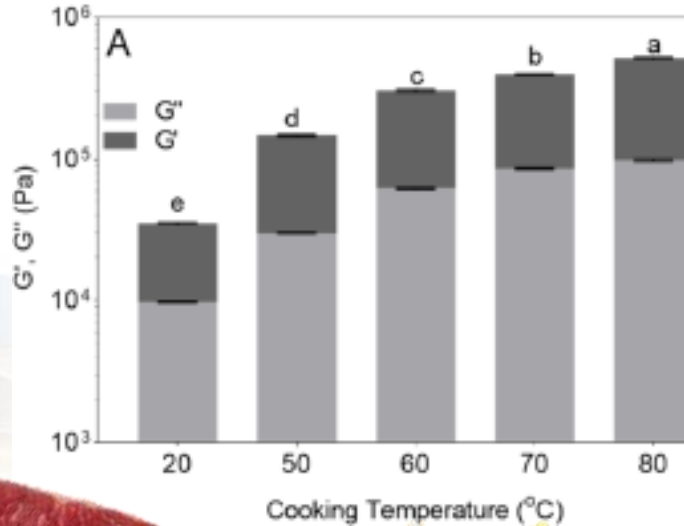
Surface area (a), and D[3,2] (c) for human breast milk and Similac™ infant formulas and correlations between surface area (b) and D[3,2] (d) against bioaccessibility





# Beef vs Plant-Based Burgers

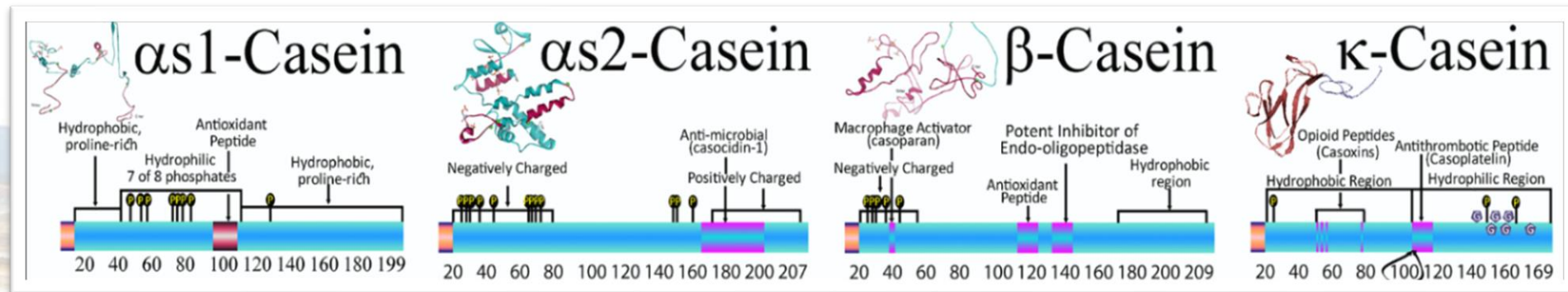
AAA boneless beef striploin





# Ending Where We Started – Co-evolution with Diet

## Milk the abomasum



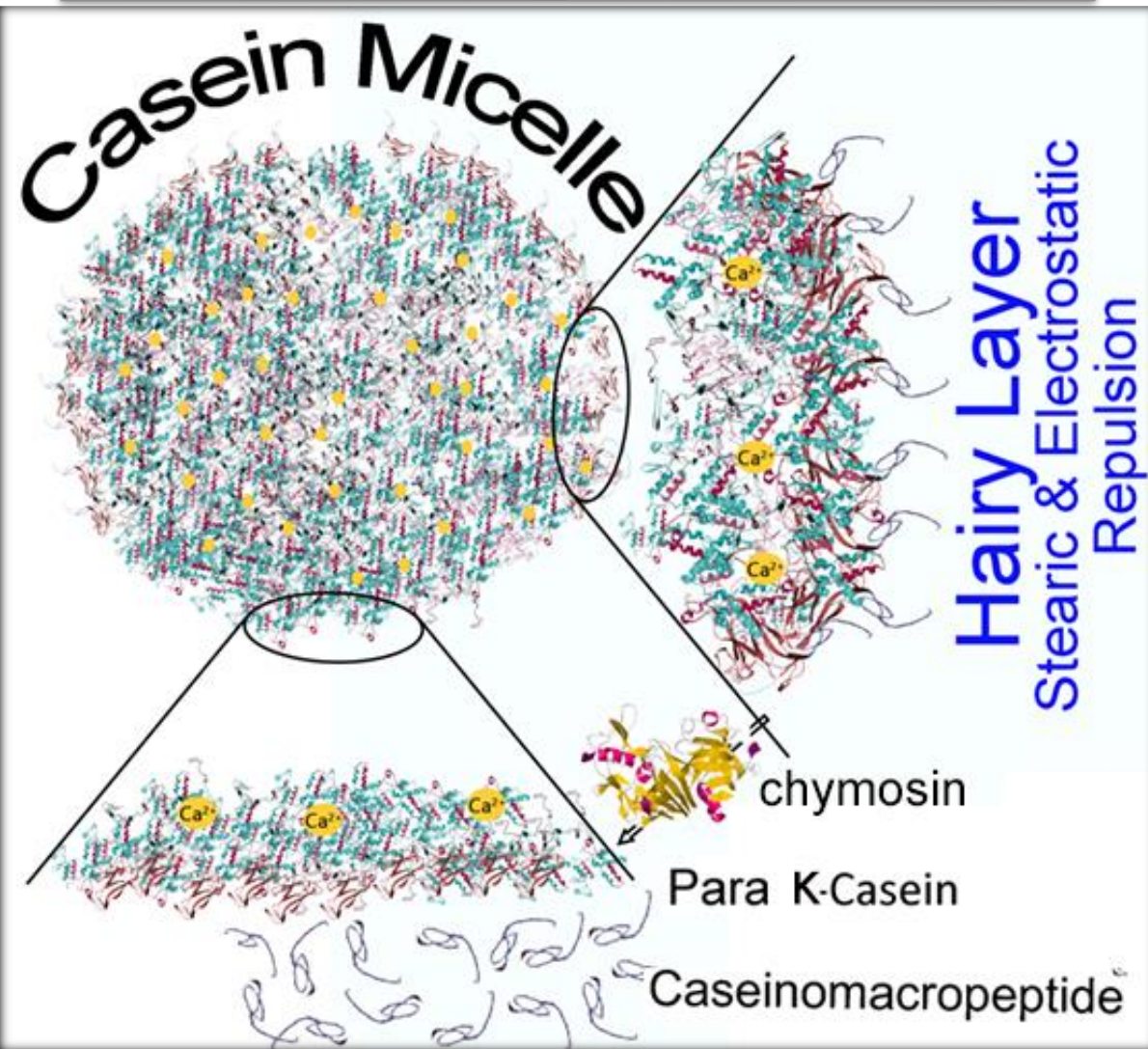
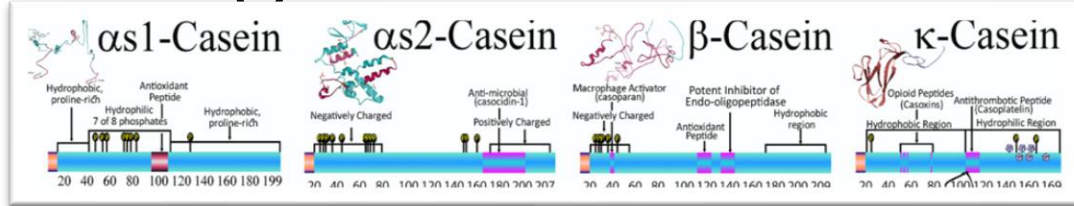
## Milk Protein - Caseins

- **$\alpha_{s1}$ -casein:** Two hydrophobic regions contain all the proline residues and is separated by a polar region, which contains all but one of eight phosphate groups
- **$\alpha_{s2}$ -casein:** Concentrated negative charges near N-terminus and positive charges near C-terminus
- **$\beta$ -casein:** Very amphiphilic protein and less sensitive to  $\text{Ca}^{2+}$  precipitation
- **$\kappa$ -casein:** Resistant to  $\text{Ca}^{2+}$  precipitation and amphiphilic stabilizes caseins



# Ending Where We Started – Co-evolution with Diet

Milk the abomasum



## Casein Micelle Formation

- $\text{Ca}^{2+}$  neutralizes charges of phosphate clusters of  $\alpha_{s1}$  &  $\alpha_{s2}$  casein
- K-casein is amphiphilic and resides at interface
  - Extends into aqueous phase and prevents coalescence
- $\text{Ca}^{2+}$  in milk  $\sim 1200$  mg/L
- $\text{Ca}^{2+}$  in water  $\sim 14$  mg/L

# Ending Where We Started – Co-evolution with Diet

## Milk the abomasum



### Prochymosin zymogen



↓pH

### Chymosin enzyme



- High pH & presence of milk induces secretion of abomasa acid, (slowly acidifies)
- Chymosin, the active aspartic protease, forms in an acidic environment
- **All mammalian neonates that produce chymosin, it is newborn-specific gastric peptidase and after birth, prochymosin, rapidly declines after the first two weeks**
- Afterwards pepsinogen/pepsin is the dominate digestive enzyme produced

### Prochymosin/chymosin

- Preferentially cleaves between aromatic AAs
- Highly substrate-specific (phe106-met106 on k-casein)
- Neonate pH is favors the activity of chymosin over pepsin

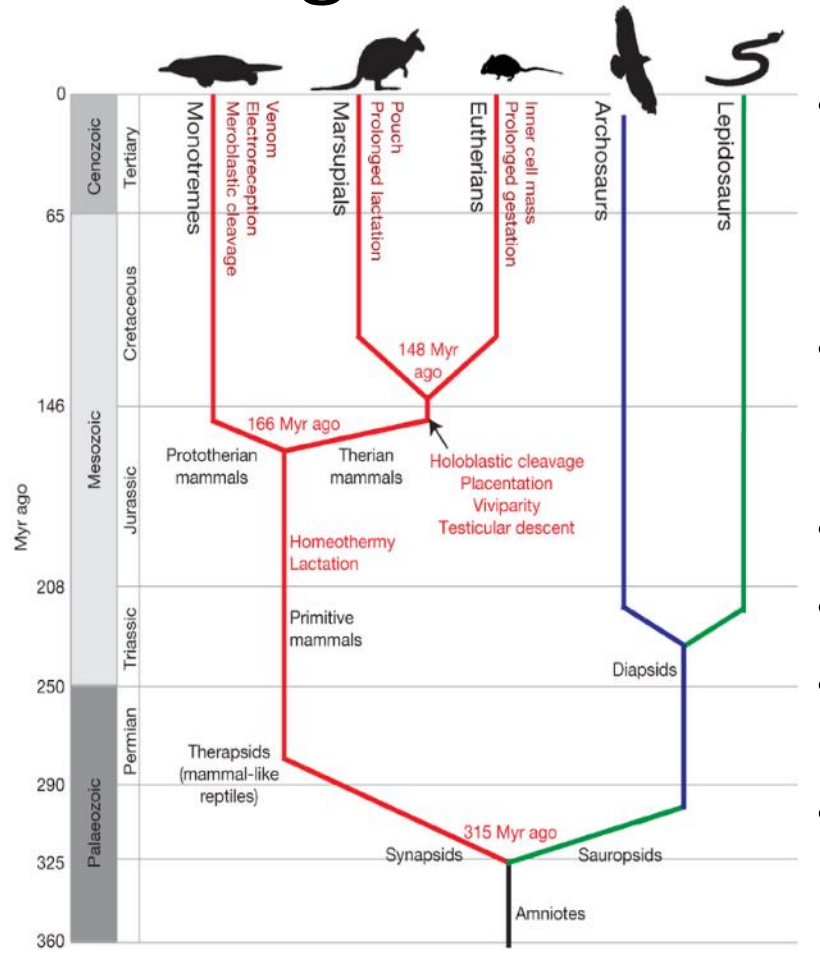
### Pepsinogen/pepsin

- Preferentially cleaves before or after aromatic AAs phenylalanine, tyrosine, tryptophan, and leucine
- The biological gain of pepsin is to hydrolyze numerous AA sites producing small bioavailable peptides and AA

The biological gain of chymosin is not to 'digest' the milk protein but destabilize the micelles coagulating it into curdles of casein or cheese



# Ending Where We Started – Co-evolution with Diet



- At 166 Ma, k-casein diverged for egg-laying & therian mammals
  - Therians include eutherians (placental mammals) & marsupials k-casein have 1 or more cysteine
  - Egg-laying mammals k-casein contains no cysteine
- k-casein compositional and positional constraints appear influenced by protease evasion and protein-protein interactions
- Insertions are confined to the water-soluble fragment CMP
- para-κ-casein (PKC) length unchanged for species
- PKC length constrained to preserve stabilizing role of the micelle
- Coevolution of casein, chymosin, and calf rumen physiology favors destabilizing the hairy layer & renneting milk into cheese over full proteolysis, illustrating the role of food structure in digestion

Begs the question: Are there whole food structures, consumed for most of human evolution, that impart other advantages for humans beyond our current understanding of human nutrition?



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# Conclusions

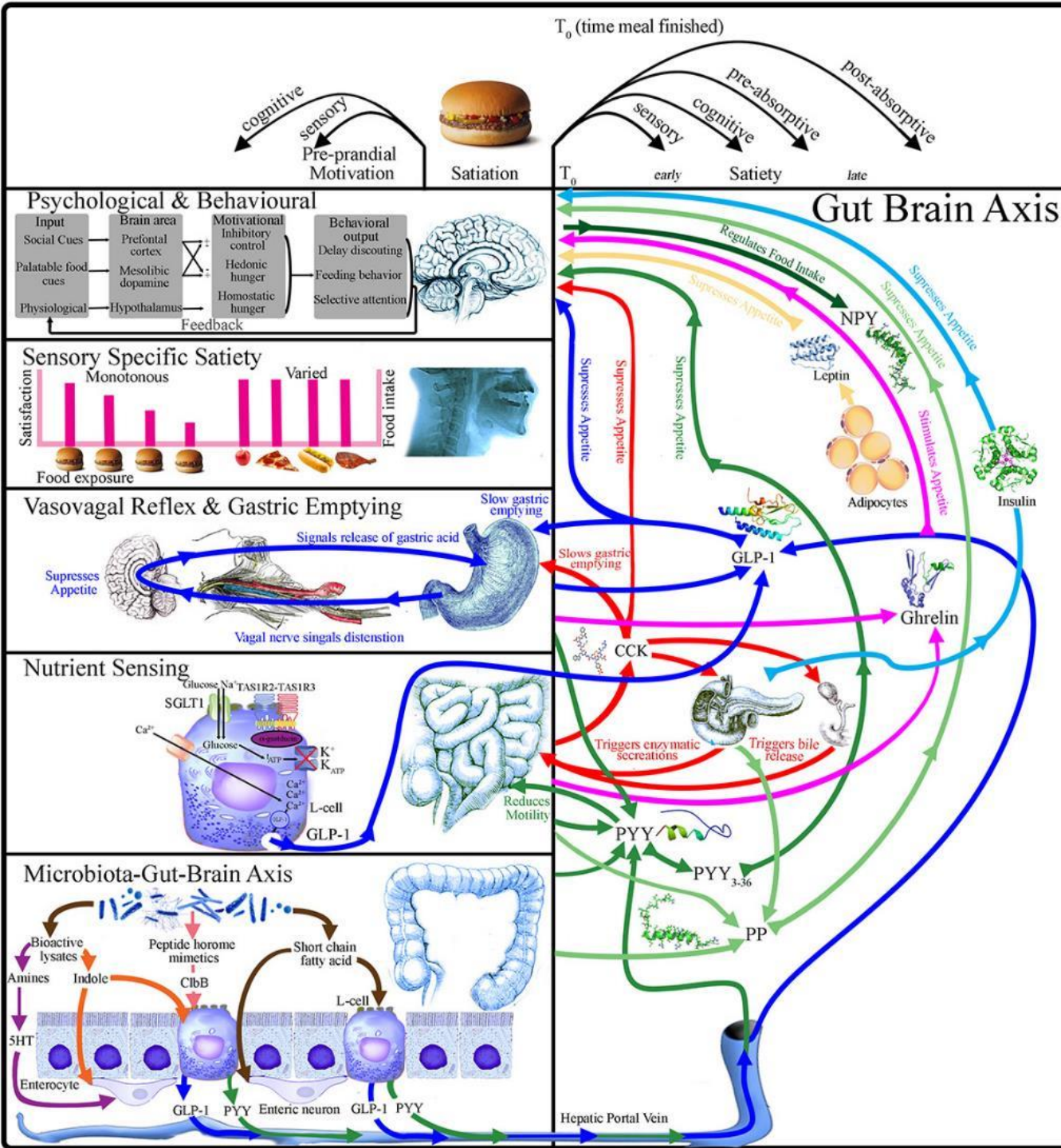
- Ultra-processed plant-based burgers do not digest the same as meat and are not nutritionally similar
- The difference in **nutritional composition** and **nutrient abundance** between beef and plant-based burgers alters the **gut microbiota profile** and **SCFA %** in the TWINSHIME; yet; composition alone fails to account for distinctly **different physical structures**, leading to **altered macronutrient digestion kinetics in the TIM-1**
- **Whole foods are not equivalent to ultra-processed formulated foods**
- **Diets high in ultra-processed foods have deleterious health outcomes compared to diets high in whole foods**

Thank you for your attention

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Others

## Questions?

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