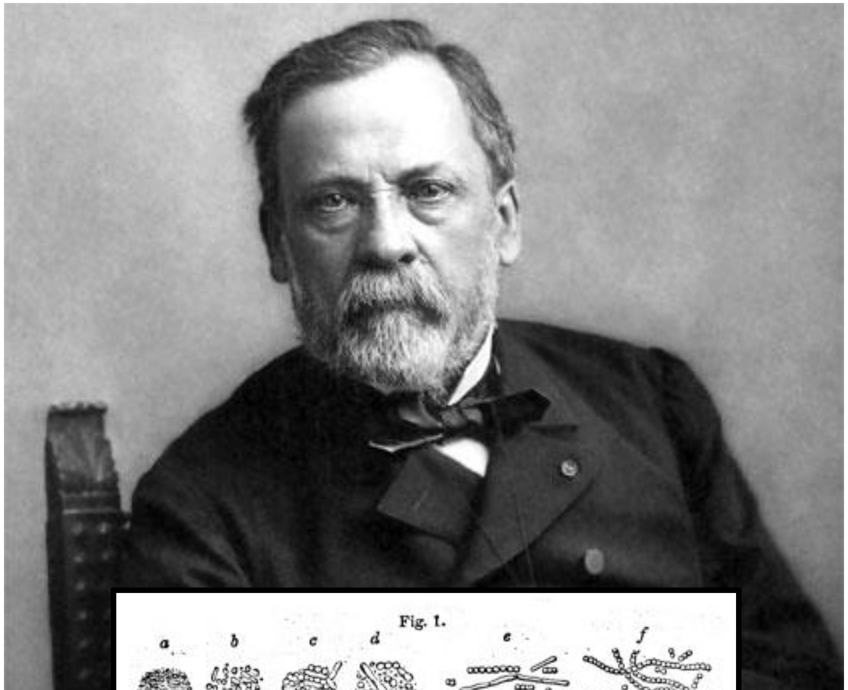
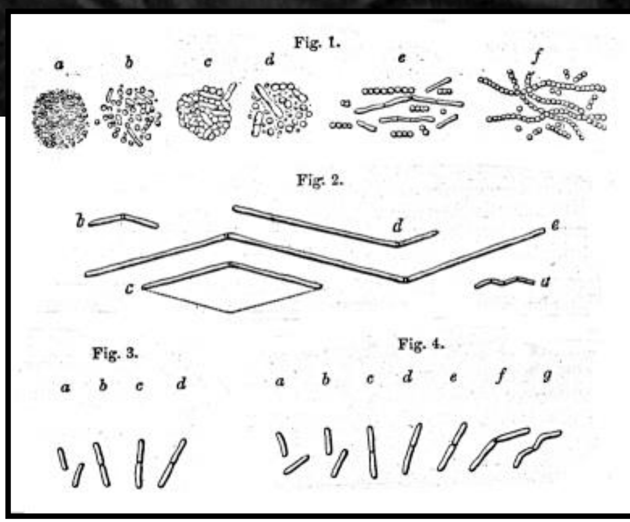
Fermentation, fermented products and probiotics

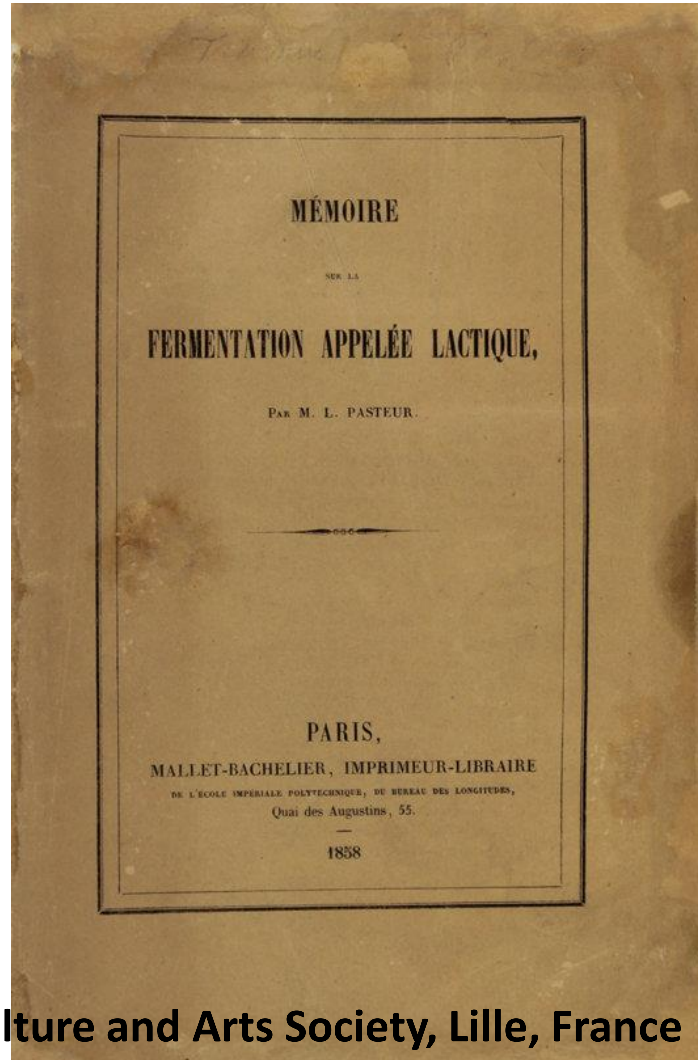
Dr. Gabriel Vinderola

Investigador Independiente CONICET
Instituto de Lactología Industrial (INLAIN, UNL-CONICET)
Profesor Asociado, Cátedra de Microbiología
Departamento de Ingeniería de Alimentos
Facultad de Ingeniería Química
Universidad Nacional del Litoral, Santa Fe
gvinde@fiq.unl.edu.ar

The anecdote







MÉMOIRE

SUR LA

FERMENTATION APPELÉE LACTIQUE,

PAR M. L. PASTEUR.

PARIS,

MALLET-BACHELIER, IMPRIMEUR-LIBRAIRE

DE L'ÉCOLE IMPÉRIALE POLYTECHNIQUE, DU BUREAU DES LONGITUDES,

Quai des Augustins, 55.

1858

Birth of Microbiology

Session of August 8th, 1857 at the Sience, Agriculture and Arts Society, Lille, France

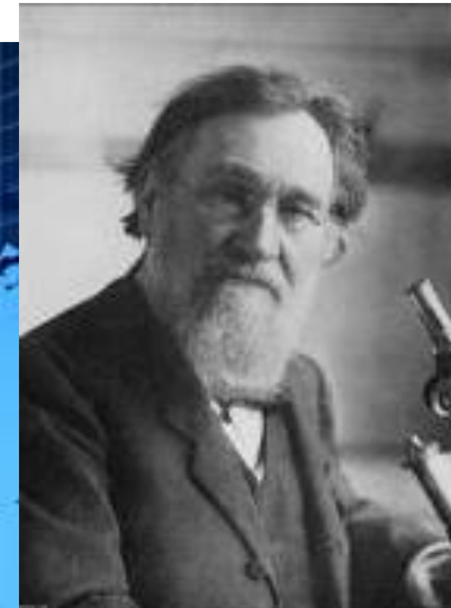








Elías Metchnikoff (1845, Ucrania – 1916, France).
Inmunologist, microbiologist, physician.
Mobel Prize in Medicin 1908.




THE PROLONGATION OF LIFE

OPTIMISTIC STUDIES

ÉLIE METCHNIKOFF

THE ENGLISH TRANSLATION

EDITED BY

P. CHALMERS MITCHELL

G. P. PUTNAM'S SONS
NEW YORK & LONDON
The Knickerbocker Press

¨The regular intake of fermented milks is associated with an enhanced health state and longer longevity. Aging is due to putrefactive bacteria in the gut, and can be delayed by lactic acid¨

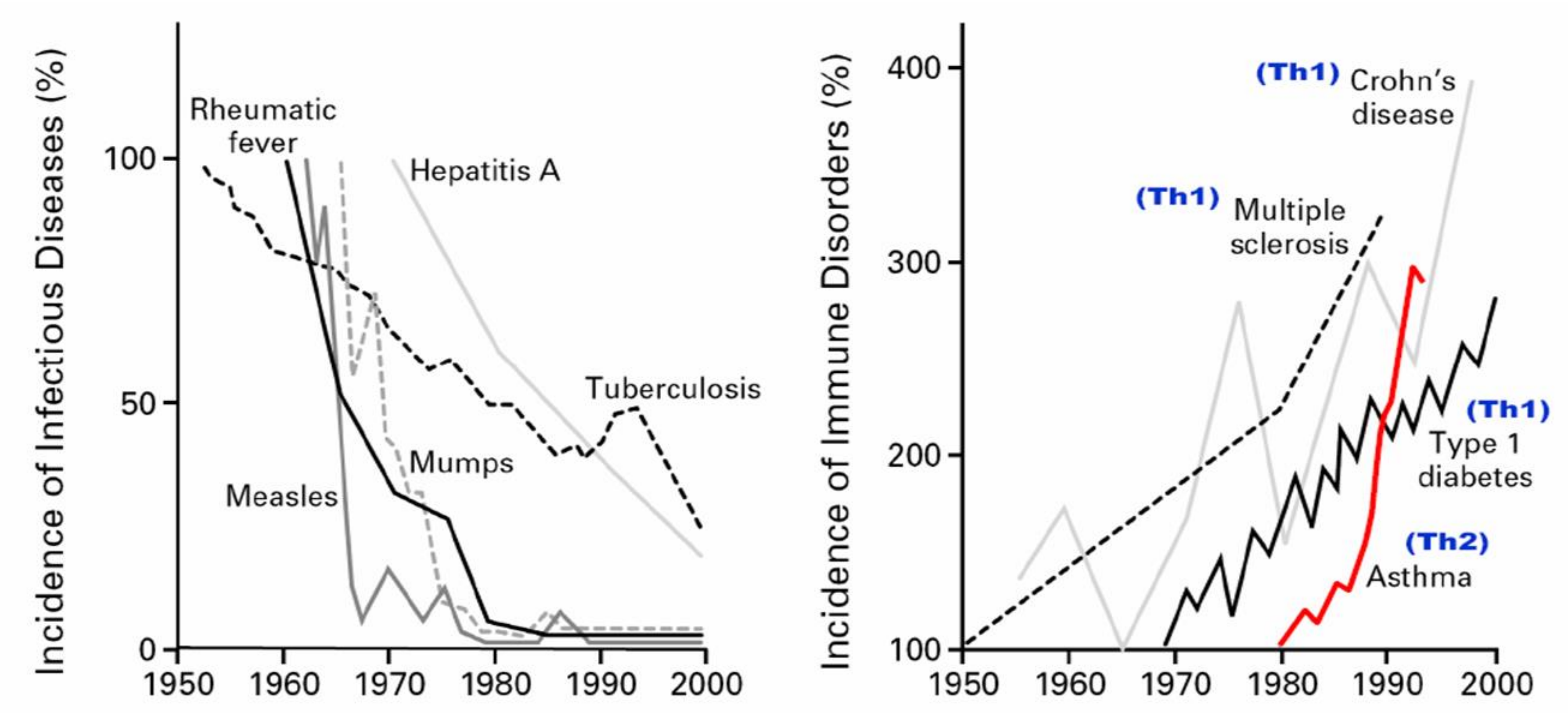
Bulgarian peasants Baba Vasilka at 126 years and her son Tudor, 101.They are typical examples of people who lived to a great age by the use of soured milk.

Why is it necessary to consume live bacteria?

Modern life gradually reduced our natural contact with microbes…

Desinfectants Antiseptics Antibiotics
Urban life Pasteurization Western diet

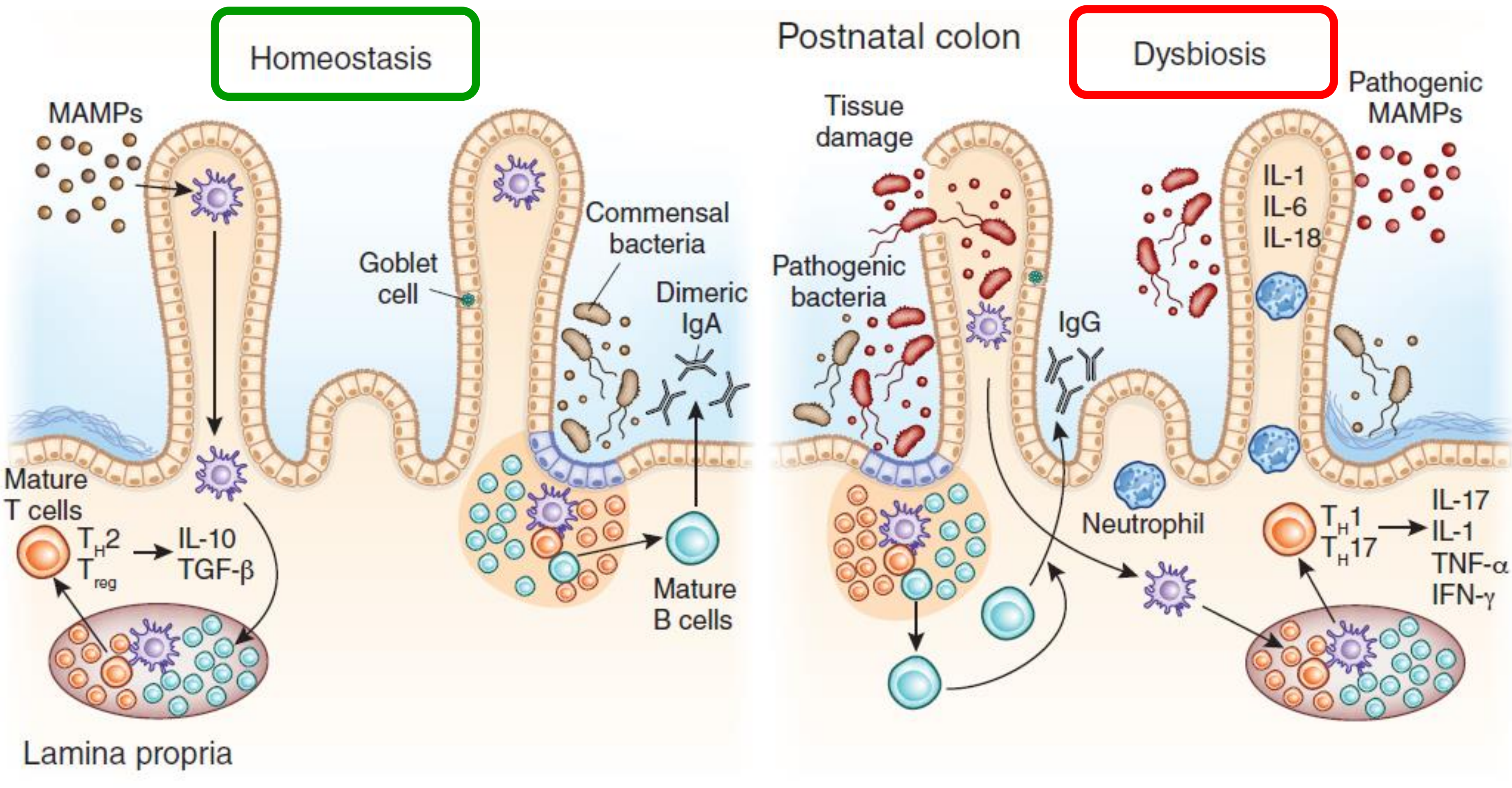
The effect of infections on susceptibility to autoimmune and allergic diseases. Bach JF. N Engl J Med. 2002 Sep 19;347(12):911-20.



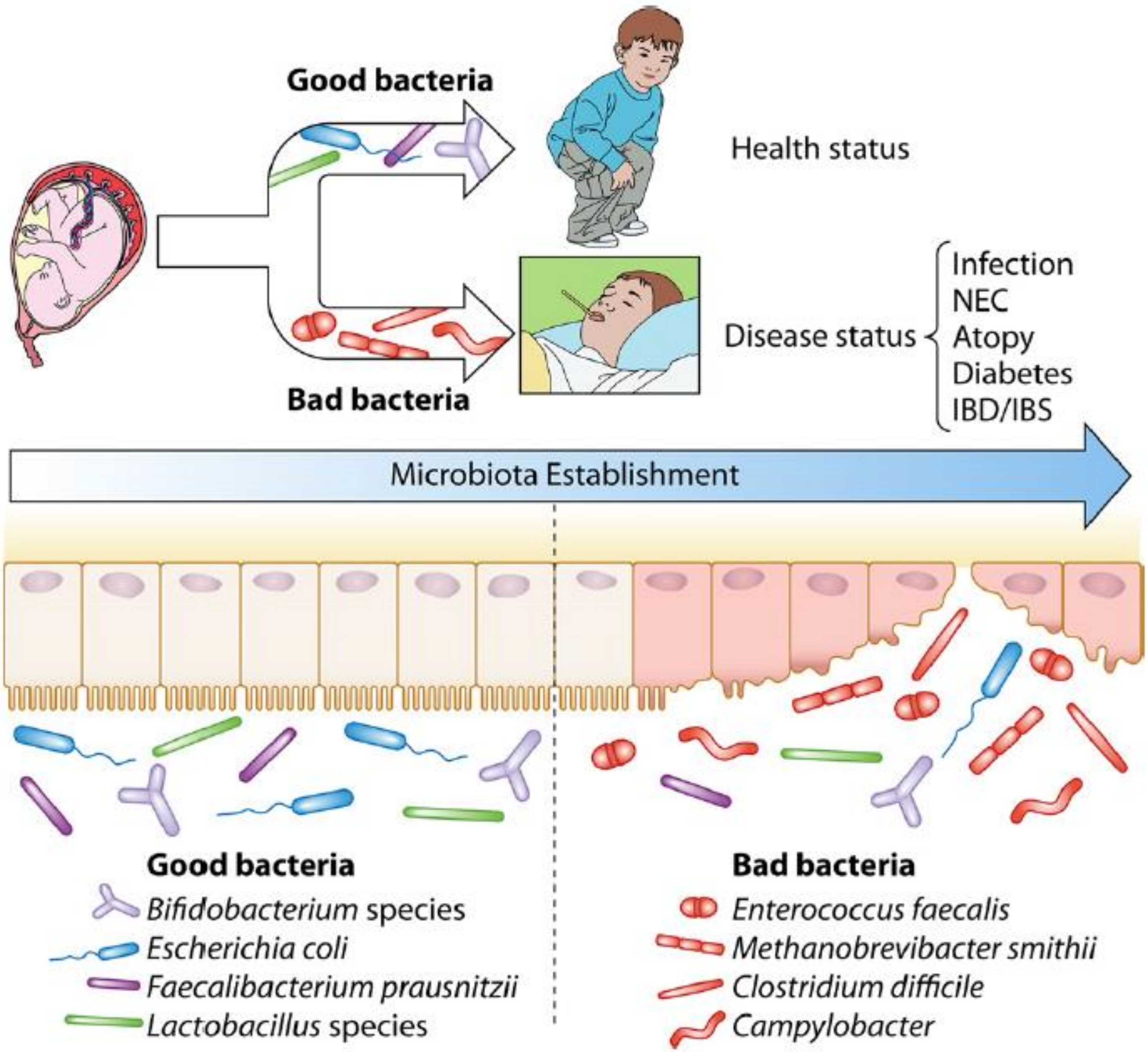
Bach. N Eng J Med. 2002. 347:911

This review examines the evidence in support of the **hygiene hypothesis** and offers a number of mechanisms that could explain the **relation between sanitary conditions and susceptibility to allergic and autoimmune diseases**.

First come, first served: early colonization shape the immune response of our gut (oral tolerance).



Milani et al. 2017, Microbiol Mol Biol Rev. 81(4)



Microbes put the gut immnune system to work

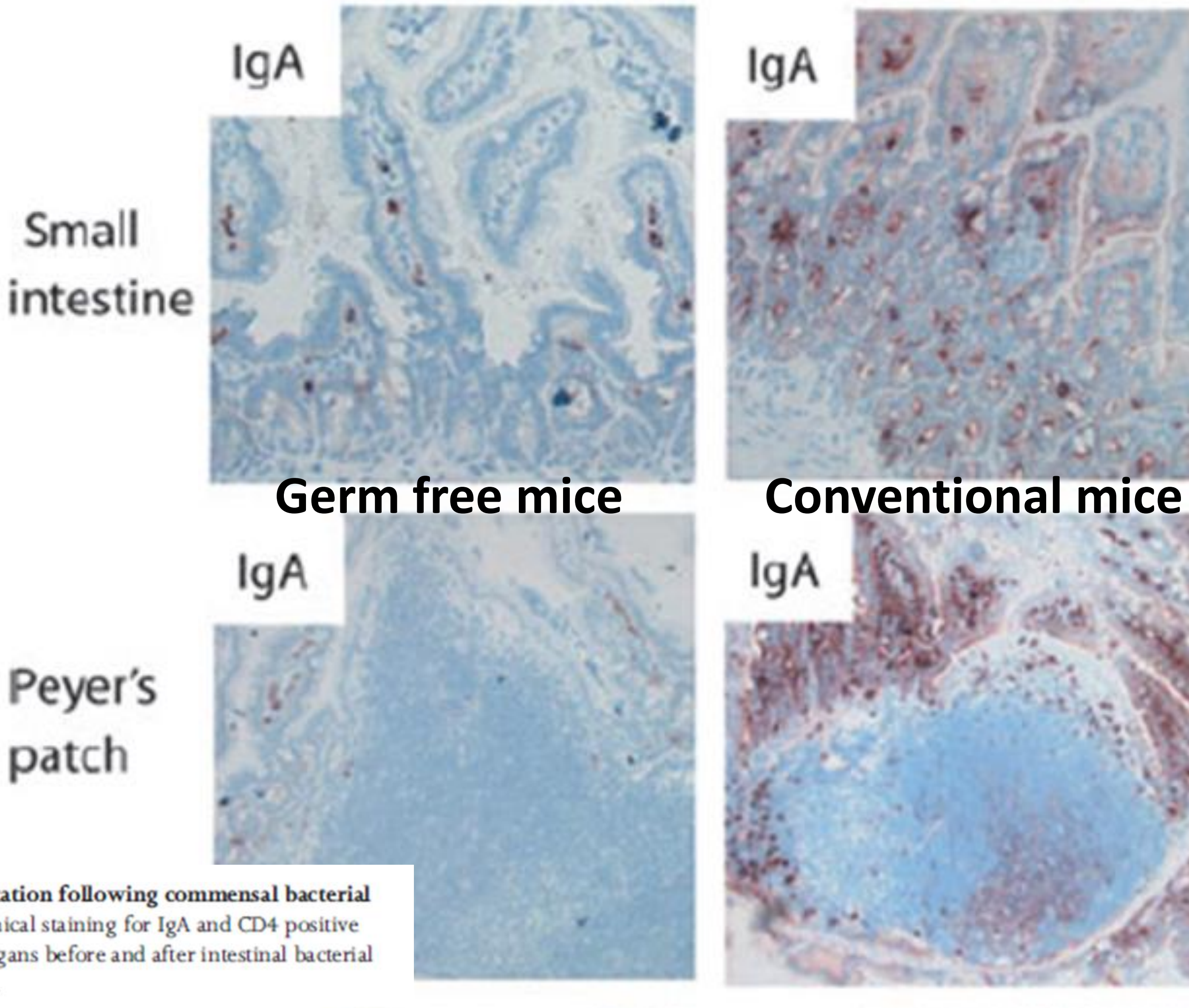


Fig. 1. Intestinal immune adaptation following commensal bacterial colonization. Immunohistochemical staining for IgA and CD4 positive cells is shown in the indicated organs before and after intestinal bacterial colonization. Adapted from (11).

Journal of Dairy Research (2006) 73 492–498. © *Proprietors of Journal of Dairy Research 2006*
doi:10.1017/S0022029906002068 *Printed in the United Kingdom*

Dietary deprivation of fermented foods causes a fall in innate immune response. Lactic acid bacteria can counteract the immunological effect of this deprivation

Mónica Olivares[1]*, Mª Paz Díaz-Ropero[1], Nuria Gómez[1], Saleta Sierra[1], Federico Lara-Villoslada
Rocío Martín[2], Juan Miguel Rodríguez[2] and Jordi Xaus[1]

[1] Immunology and Animal Science Department, Puleva Biotech SA, 18004 Granada, Spain
[2] Departamento de Nutrición y Bromatología III, Universidad Complutense de Madrid, 28040 Madrid, Spain

Received 13 October 2005 and accepted for publication 22 March 2006

People that consume FF (> 5 times/week), when removed from diet, a diminution in the phagocytic activity and the concentration of SCFA is observed. Restored activity when yoghurt or yoghurt with probiotics are incorporated in the diet.

counteracted the fall in the immune response, although the probiotic product was more effective than the standard yogurt.

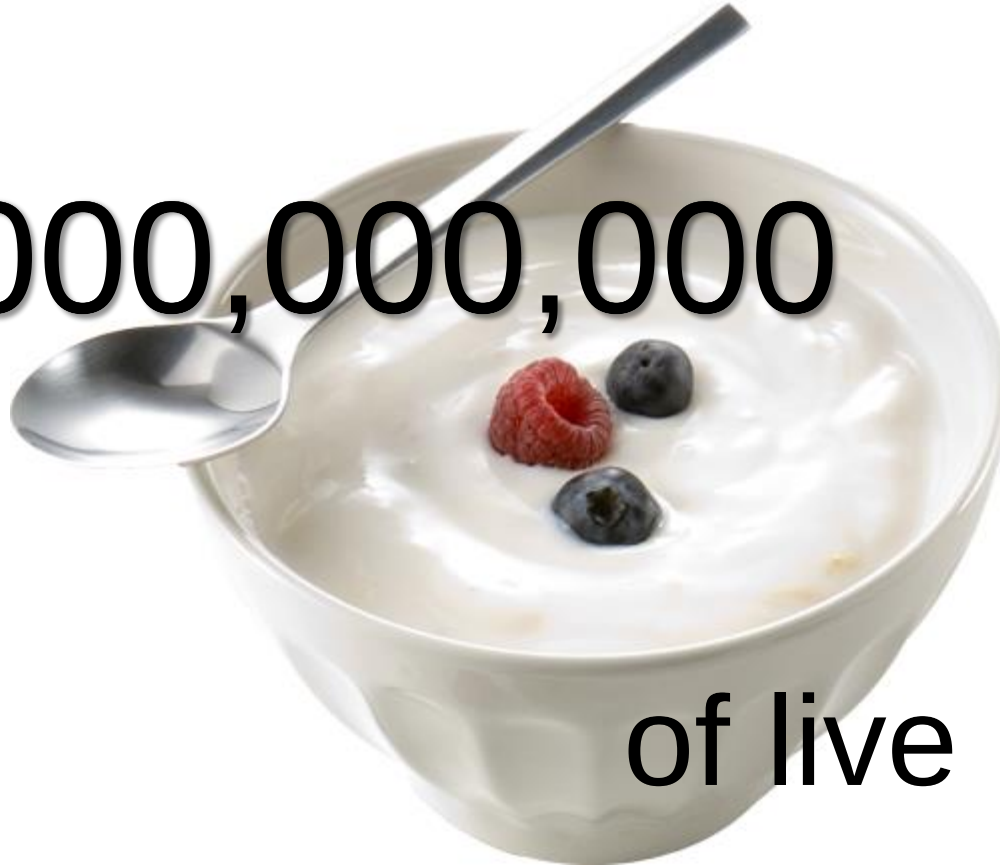
How many microbes do we get every day in our food?

Dietary pattern	Meal	Aerobic plate count	Anaerobic plate count	Yeast count	Mold count	Total microorganisms
Average American	Breakfast	2.15E+05	2.26E+05	5.66E+02	5.66E+03	4.48E+05
	Lunch	2.23E+05	1.31E+04	1.31E+03	1.31E+03	2.38E+05
	Snack	1.87E+04	2.34E+03	2.34E+02	2.34E+02	2.15E+04
	Dinner	1.47E+05	5.35E+05	7.75E+02	7.75E+02	6.84E+05
	Total	6.04E+05	7.77E+05	2.88E+03	7.98E+03	1.39E+06
USDA recommended	Breakfast	1.14E+04	5.72E+02	4.29E+04	1.49E+06	1.54E+06
	Snack #1	2.11E+05	5.42E+07	5.42E+02	1.19E+05	5.45E+07
	Lunch	3.25E+07	2.26E+06	1.06E+06	2.55E+06	3.84E+07
	Snack #2	5.54E+08	6.09E+08	3.32E+04	1.39E+04	1.16E+09
	Dinner	3.49E+05	5.81E+04	9.69E+02	9.69E+03	4.17E+05
	Total	5.87E+08	6.66E+08	1.14E+06	4.18E+06	1.26E+09
Vegan	Breakfast	3.38E+04	1.99E+04	3.98E+02	9.95E+03	6.41E+04
	Snack #1	1.97E+06	1.67E+06	5.41E+05	4.92E+05	4.67E+06
	Lunch	1.22E+05	2.34E+04	9.35E+02	9.35E+02	1.47E+05
	Snack #2	9.81E+04	4.67E+03	3.50E+04	2.80E+05	4.18E+05
	Dinner	4.07E+05	1.45E+05	4.53E+02	9.05E+03	5.62E+05
	Snack #3	1.43E+05	2.94E+03	8.40E+01	8.40E+01	1.46E+05
	Total	2.77E+06	1.87E+06	5.78E+05	7.92E+05	6.01E+06

The microbes we eat: abundance and taxonomy of microbes consumed in a day's worth of meals for three diet types. Lang et al., Peer J. 2014 Dec 9;2:e659. doi: 10.7717/peerj.659.

A yoghurt every day provides

1,000,000,000



# of live microbes

Que cantidad de microorganismos comemos al día?

Dietary pattern	Meal	Aerobic plate count	Anaerobic plate count	Yeast count	Mold count	Total microorganisms
Average American	Breakfast	2.15E+05	2.26E+05	5.66E+02	5.66E+03	4.48E+05
	Lunch	2.23E+05	1.31E+04	1.31E+03	1.31E+03	2.38E+05
	Snack	1.87E+04	2.34E+03	2.34E+02	2.34E+02	2.15E+04
	Dinner	1.47E+05	5.35E+05	7.75E+02	7.75E+02	6.84E+05
	Total	6.04E+05	7.77E+05	2.88E+03	7.98E+03	1.39E+06
USDA recommended	Breakfast	1.14E+04	5.72E+02	4.29E+04	1.49E+06	1.54E+06
ChooseMyPlate.gov	Snack #1	2.11E+05	5.42E+07	5.42E+02	1.19E+05	5.45E+07
	Lunch	3.25E+07	2.26E+06	1.06E+06	2.55E+06	3.84E+07
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The microbes we eat: abundance and taxonomy of microbes consumed in a day's worth of meals for three diet types. Lang et al., Peer J. 2014 Dec 9;2:e659. doi: 10.7717/peerj.659.

Nature. 2013 Aug 1;500(7460):20-2. doi: 10.1038/500020a.

Archaeology: The milk revolution.

Curry A.

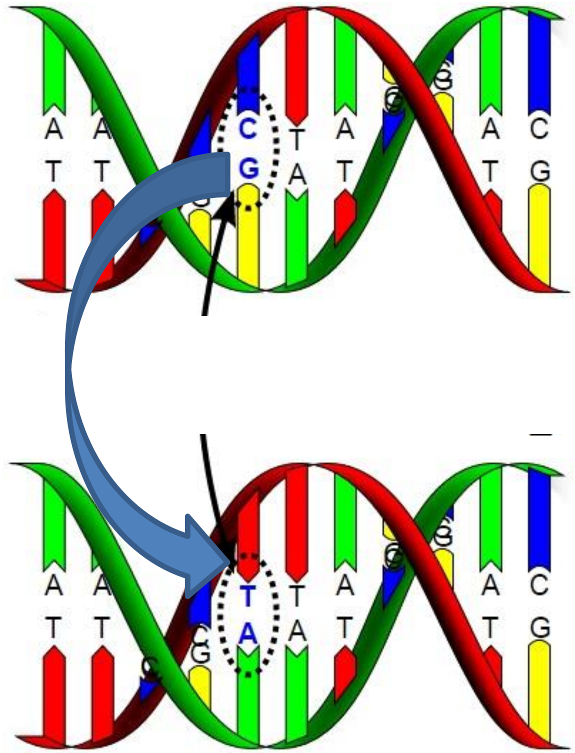
The milk revolution

When a single genetic mutation first let ancient Europeans drink milk, it set the stage for a continental upheaval.

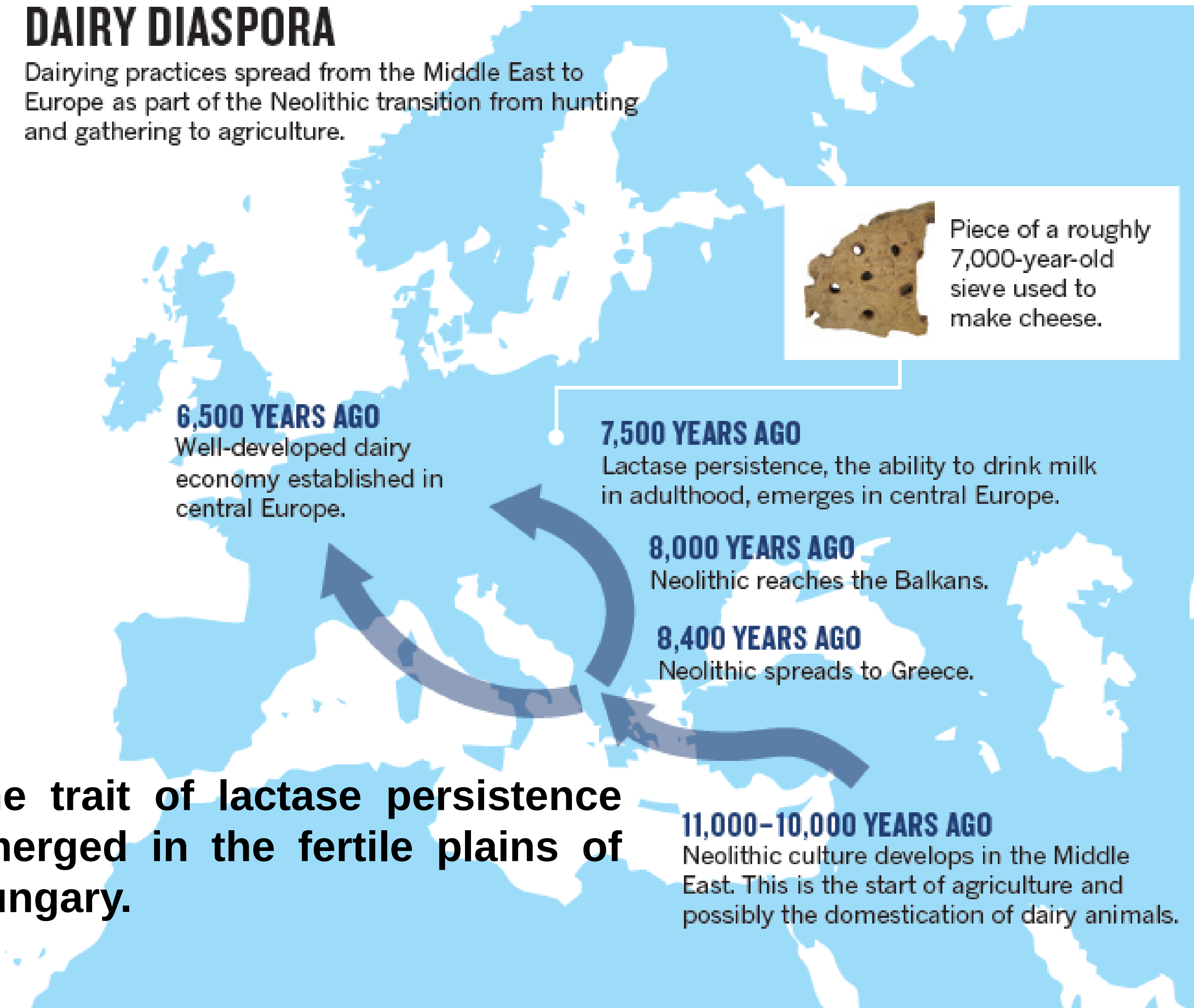
By the end of the last **Ice Age** (20,000-12,000 years ago) milk was still essentially a toxin to human adults.

As farming started to replace hunting and gathering in the Middle East (11,000 years ago), cattle herders **learned how to reduce lactose** to tolerable levels for adults by fermenting milk.

A single nucleotide mutation 7500 years ago: a cytosine changed to thymine in a genomic region not far from the lactase gene.



The mutation gave adults the ability to produce lactase beyond childhood and drink milk. That adaptation opened up a source of nutrition that could have sustained communities when harvests failed.



The trait of lactase persistence emerged in the fertile plains of Hungary.

Fermented milks evolved to different varieties around the world

Table 1.1 Yogurt and Yogurt-Like Products From Around the World

Traditional Name	Country	Traditional Name	Country
Busa	Turkestan	Mezzoradu	Sicily
Cieddu	Italy	Roba	Iraq
Dahi/Dadhi/Dahee	India, Bangladesh, Nepal	Skyr	Iceland
Filmjolk/Fillbunke/ Filbunk/Surmelk/	Scandinavia	Taettem-jolk/Tettemelk Tarho	Hungary
Gioddu	Sardinia	Tiaourti	Greece
Jugurt/Eyran	Turkey	Urgotnic	Balkan Mountains
Katyk	Transcaucasia	Villi	Finland
Kissel Mleka	Balkans	Yogurt/Yogurt/Yaort	Rest of the world
Leben/Leban	Lebanon and some Arab countries	Yourt/Yaourti/Yahourth/ Yogur/Yaghourt	("Y" is replaced by "J" in some instances)
Mast/Dough	Iran and Afghanistan		
Mazun/Matzoon	Armenia	Zabady	Egypt and Sudan

Adapted from Tamime, A.Y., Deeth, H.C., 1980. Yoghurt: technology and biochemistry. J. Food Prot. 43 (2), 939–977; Kosikowski, F., Mistry, V.V., 1997. Fermented Milk Foods-Origins and Principles, vol. 1. F.V. Kosikowski-L.L.C., Westport, CT, USA, pp. 87–108.

Diversity of microbes in the different fermented milks

Ayran (yoghurt from goat milk)	Turkey	*L. plantarum*, *L. brevis* *L. paracasei* subsp. *paracasei*, *L. casei* subsp. *pseudoplantarum*
Gioddu, traditional fermented sheep or goat milk	Sardinian, Italy	*S. thermophilus*, *L. lactis subsp. lactis* *L. delbrueckii subsp. bulgaricus*, *L. casei subsp. casei*, *L. mesenteroides subsp. mesenteroides*
Tarag	Mongolia	*L. helveticus*, *L. lactis* subsp. *lactis*, *L.casei*
Fermented milk	Japan	*L. casei* strain Shirota
Koumiss from mare's milk	Italy	*L. delbrueckii* subsp. *bulgaricus S. thermophilus*
Lben	Marocco	Spontaneously/not identified
Functional fermented milk	Italy	*L. lactis* DIBCA2, *L. plantarum* PU11
Kumis	West Colombia	*E. faecalis*, *E. faecium*
Ewe milk, traditional yoghurt	Iran	*L. brevis*
Maasai	Kenya	*L. plantarum*, *L. fermentum*, *L. acidophillus*, *L. paracasei*
Suusac	Kenya	*L. curvatus*, *L. plantarum*, *L. salivarius*, *L. raffinolactis* *Leuconostoc mesenteroides subsp. mesenteroides.*

Animal containers

Plant containers

From artisanal fermented milks to commercial yoghurt

Lactobacillus plantarum
Lactobacillus acidophilus
Streptococcus thermophilus
Lactobacillus bulgaricus
Lactobacillus reuteri
Lactobacillus casei
Bifidobacterium
Lactococcus lactis
Leuconostoc mesenteroides
Lactobacillus rhamnosus

Streptococcus thermophilus
Lactobacillus bulgaricus

probiotics

What is yoghurt?

What is fermentation?

Who ferments milk?

How is yoghurt produced?

What happens to milk components?

Argentinian Food Code

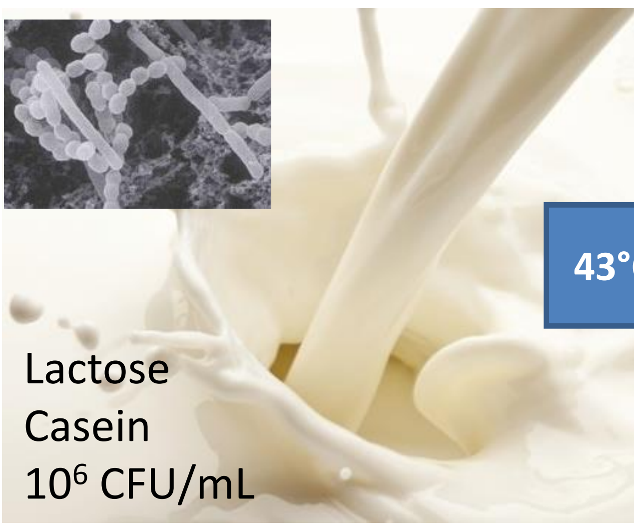
Artículo 576 - (Resolución Conjunta SPRyRS y SAGPyA N° 33/2006 y N° 563/2006)

1) Definiciones: Se entiende por Leches Fermentadas los productos, adicionados o no de otras sustancias alimenticias, obtenidos por coagulación y disminución del pH de la leche o leche reconstituida, adicionada o no de otros productos lácteos, por fermentación láctica mediante la acción de cultivos de microorganismos específicos. Estos microorganismos específicos deben ser viables, activos y abundantes en el producto final durante su período de validez.

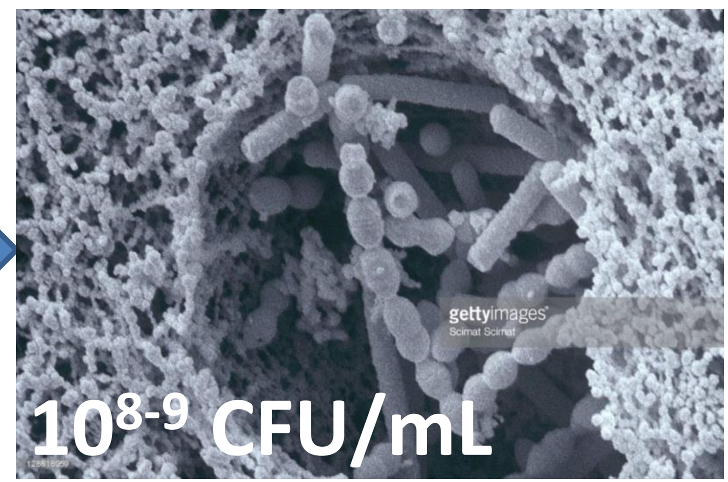
1.1) Se entiende por Yogur o Yoghurt o Iogurte, en adelante Yogur, el producto incluido en la definición 1) cuya **fermentación** se realiza con cultivos protosimbióticos de *Lactobacillus delbrueckii* subsp. *bulgaricus* y *Streptococcus salivarius* subsp. *thermophilus* (**fermentos**) a los que en forma complementaria pueden acompañar otras bacterias acidolácticas (**probióticos?**) que, por su actividad, contribuyen a la determinación de las características del producto terminado.

Lactic acid fermentation of milk

Metabolic process carried out by *Streptococcus thermophilus* and *Lactobacillus bulgaricus* in pasteurized milk. Partial consumption of certain milk nutrients, breakdown of proteins, increase of biomass (100-1000 folds), production of bioactive metabolites y transformation of reological (clotting, viscosity) and sensorial properties.

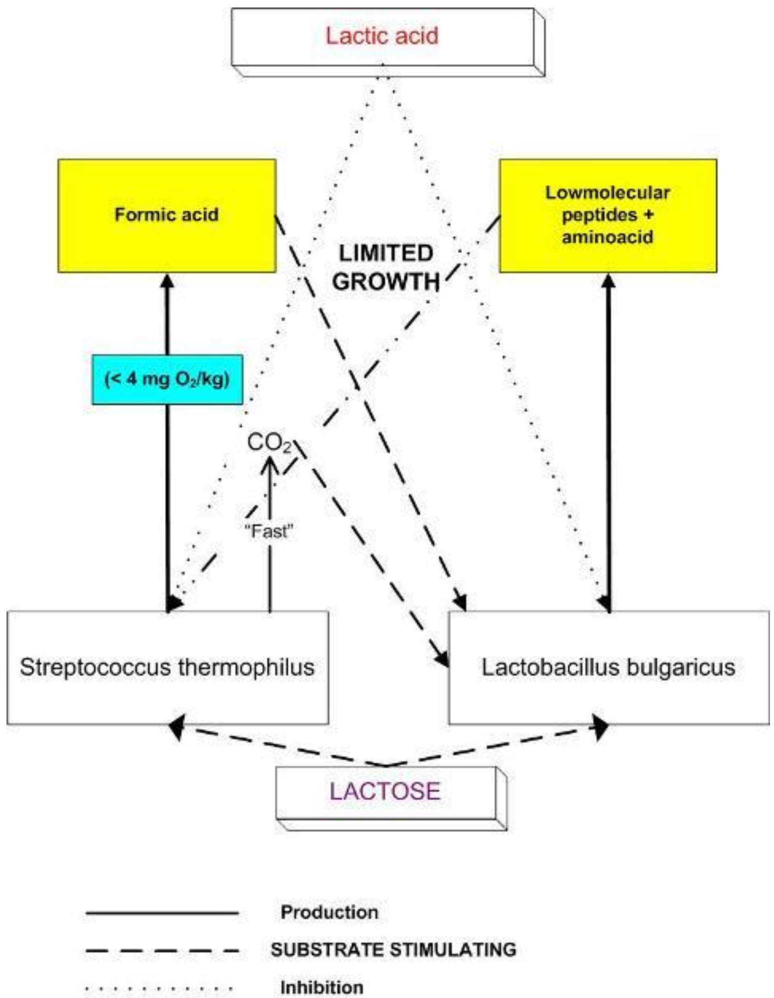


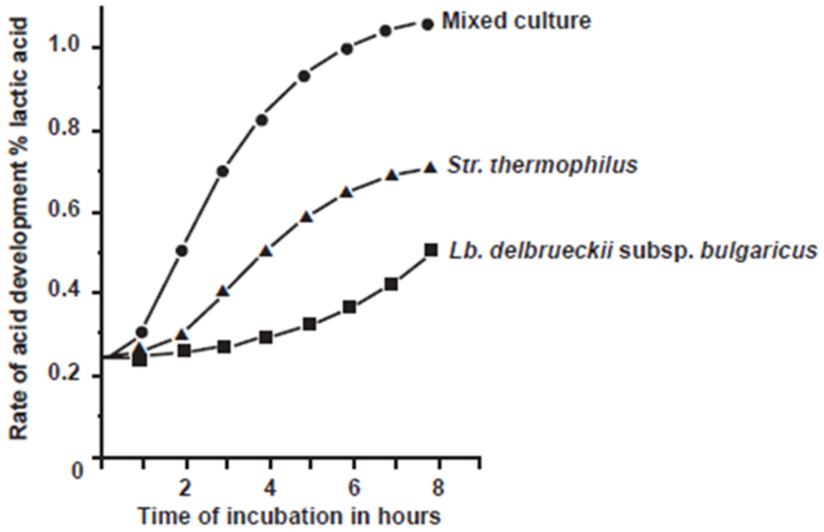
43°C , 4– 5 h

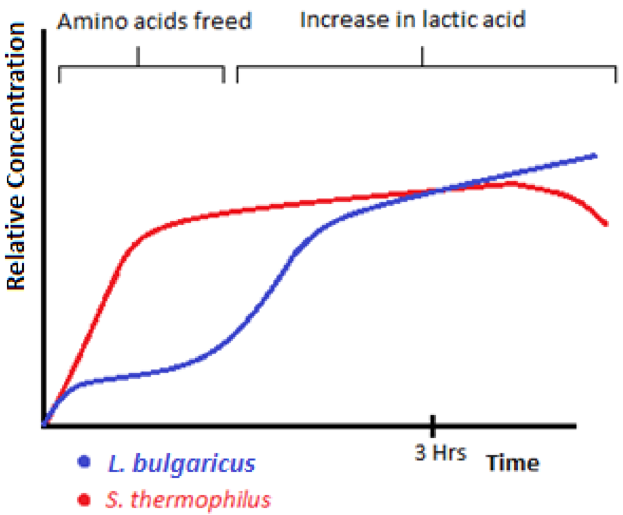


< Lactose, > peptides, lactic acid, bacteriocins, aroma compounds, exopolysaccharydes.

Protocooperation: unique symbiosis between *S. thermophilus* and *L. bulgaricus* in milk.







How is yoghurt manufactured?

1) Mixture of ingredients (total solids).
2) Heat treatment and homogenization.
3) Inoculation of starters (*S. thermophilus* y *L. bulgaricus*).
4) Incubation 43°C for 4-5 h (↓pH).
5) Cooling and packaging.
6) Distribution to retailers.

What happens to milk components?

Some vitamins are consumed by LAB, mainly those of the B group. However, there is are small changes in overall content.

Minor changes en mineral content: possible increased Ca availability due to lower pH (high absorptive rate).

Lactose is hydrolized and sugars consumed (from 4.5% to 3-3.5%), and further hydrolized during GIT transit (microbial lactase).

Antimicrobial agents produced: organic acids, hydrogen peroxide, bacteriocins. Exopolysaccharides (inmmunomodulator).

Desnaturalization/Hydrolysis of allergenic proteins. Enhanced digestibility of total protein. Release of bioactive peptides.

Milk as a source of bioactive peptides

- **Caseins harbor > 20.000 different peptides sequences.**
  - **The OTS allows the entry of peptides < 11-18 aa.**
- **< 25% of the peptides released are used for growth.**

Yoghurt is an important reservoire of bioactive peptides

Multiple biological activity of milk peptides

JOURNAL OF FUNCTIONAL FOODS 1 (2009) 177–187

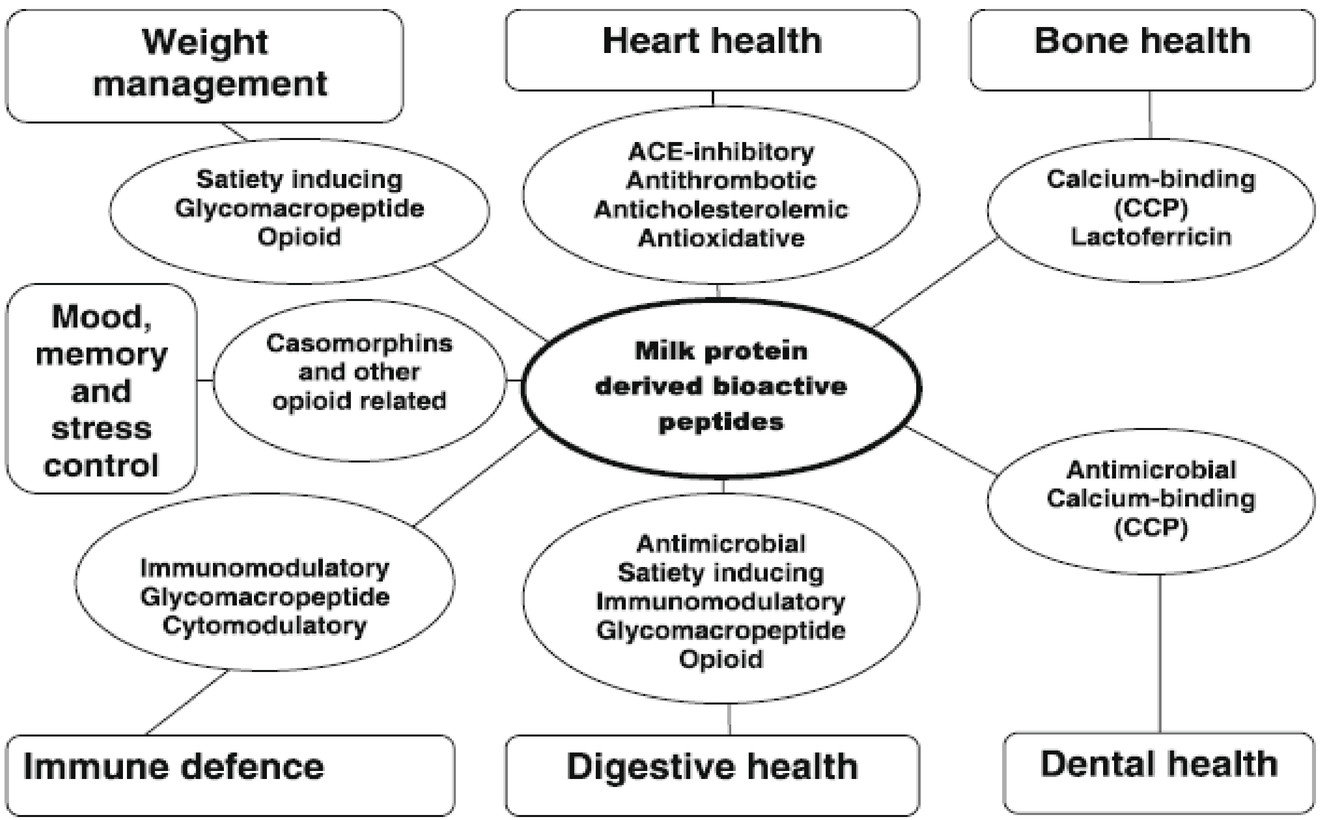


Fig. 1 – Functionality of milk protein-derived bioactive peptides and their potential health targets.

Survival of LAB starter in the gut

Table 23.1 Survival of Yogurt Starter Cultures as Measured in Human Subjects After Yogurt Ingestion and Measured by Plating Counts

	No of Treated Subjects	Yogurt Intake per Day	Daily Amount of *Streptococcus*	Survival of *Streptococcus* Cells/g Feces	Daily Amount of *Lactobacillus*	Survival of *Lactobacillus* Cells/g Feces
Brigidi et al. (2003)	5	250 g	10^8–10^{11}	4×10^5	NR	NR
del Campo et al. (2005)	114	375 g	10^{10}	None	10^9	None
Mater et al. (2005)	13	125 g	8×10^{10}	6.3×10^4	8×10^{10}	7.2×10^4 cfu/g
Elli et al. (2006)	20	250 g	5×10^9	None	6×10^9	Log 3–5.5

NR, *Not reported.*
Only papers containing data on the counts of bacteria administered in yogurt are summarized in this table.

PROBIOTICS

Live microorganisms which when administered in adequate amounts confer a health benefit on the host (FAO/WHO, 2002).

ftp://ftp.fao.org/es/esn/food/wgreport2.pdf

Major species from where probiotic strains come from:

Lactobacillus casei, *L. paracasei*, ***L. rhamnosus***, *L. acidophilus, L. gasseri, L. fermentum, …*

Bifidobacterium lactis, *B. longum, B. bifidum…*

Less used in foods:
Saccharomyces boulardii
Bacillus coagulans, B. clausii

Three aspects to be considered…

Natural inhabitants of the GIT or naturally present in artisanal fermented foods.

Lactobacilli and bifidobacteria **can be produced at large scale** for their incoorporation into foods.

They are **safe** (QPS-Europe, GRAS-USA).

Table 4.1 Examples of Probiotic Yogurts Currently on the Market and Some of the Areas of Health They Claim to Improve

Probiotic Strain	Yogurt Brand/Manufacturer	Target
Lactobacillus bulgaricus	Yoplait, Stonyfield Farms, Dannon, Fage, Greek Gods Yogurt, La Yogurt, Voskos Greek Yogurt	
Streptococcus thermophilus	Yoplait, Chobani, Stonyfield Farms, Dannon, Fage, Greek Gods Yogurt, La Yogurt, Voskos Greek Yogurt	
Bifidobacterium bifidum	Chobani, Stonyfield Farms, Fage, Greek Gods Yogurt, La Yogurt, Voskos Greek Yogurt	AAD[a]
Lactobacillus casei	Chobani, Fage, Greek Gods Yogurt, Voskos Greek Yogurt	Respiratory tract infections
Lactobacillus rhamnosus	Stonyfield Farms	Diabetes, diarrhea, AAD, improve barrier function
Bifidobacterium animalis ssp. *lactis* DN-173 010	Activia by Danone	Constipation
L. casei DN-114-001	DanActive by Danone	AAD, prevention of pediatric diarrhea, respiratory infections
L. casei Shirota	Yakult	Constipation, *H. pylori* infections
Bifidobacterium animalis BB12	La Yogurt	Eczema
L. rhamnosus GG	Vifit by Valio	Acute pediatric diarrhea, AAD
Lactobacillus reuteri DSM 17938	Protectis by BioGaia	Acute pediatric diarrhea, cholesterol

[a]AAD, *antibiotic-associated diarrhea.*

From thepoint of view of the technology of fermented milks

Starters: *S. thermophilus* and *L. bulgaricus* transform milk into yoghurt (fermentation, acidification, viscosity, hydrolisis, aroma).

Adjuncts: in general probiotics (*L. casei, L. rhamnosus, L. acidophilus,* bifidobacteria) are added before or after fermentation. They have little or no participation during fermentation..

Is it the same to consume a probiotic in a capsule or in a yoghurt?

Table 9.2 Recovery of *Lactobacillus rhamnosus* GG in stools, as a function of the delivery matrix.

Food product	**Population ingested in serving (cfu portion^{-1})**	**cfu in stools (cfu g^{-1}, wet mass)**
Powder	2×10^{10}	1×10^{6}
Fermented milk (200 ml)	1×10^{10}	3×10^{7}
Milk (200 ml)	1×10^{8}	1×10^{7}
Cheese	3×10^{8}	7×10^{7}
Fruit juice (200 ml)	2×10^{9}	1×10^{6}

60x

4000x

Table prepared from the data of Saxelin et al. (2003).

Development of Fermented Milk Products Containing Probiotics. *Claude P. Champagne.* Dairy Microbiology and Biochemistry. Recent Developments (2015). CRC Press, Taylor and Francis.

Comparative survival of LGG and LAB starter in the gut

Table 23.1 Survival of Yogurt Starter Cultures as Measured in Human Subjects After Yogurt Ingestion and Measured by Plating Counts

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Elli et al. (2006)	20	250 g	5×10^9	None	6×10^9	Log 3–5.5

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Only papers containing data on the counts of bacteria administered in yogurt are summarized in this table.

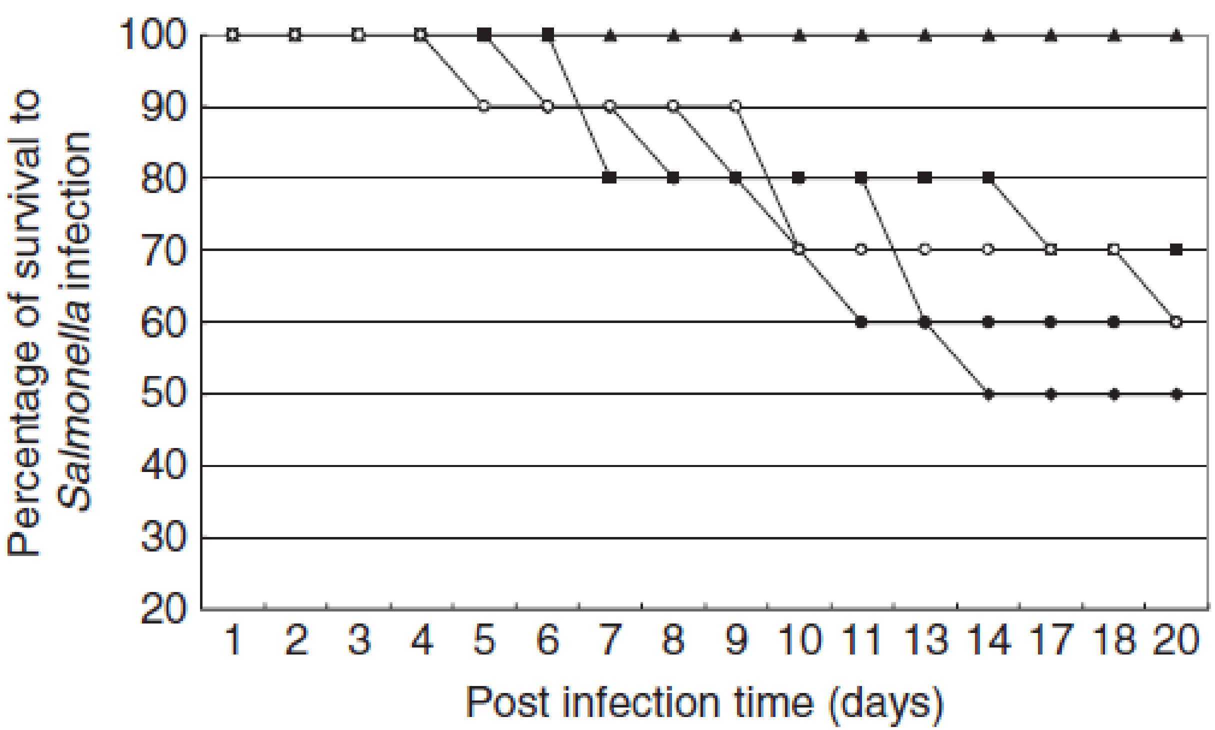
L. rhamnosus **GG survival: 4000 higher than the starters**

Journal of Applied Microbiology

Cell viability and immunostimulating and protective capacities of *Bifidobacterium longum* 5[1A] are differentially affected by technological variables in fermented milks

T.C. Souza[1], M.F. Zacarías[2], A.M. Silva[3], A. Binetti[2], J. Reinheimer[2], J.R. Nicoli[1] and G. Vinderola[2]

1 Departamento de Microbiologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil
2 Instituto de Lactología Industrial (INLAIN, UNL-CONICET), Facultad de Ingeniería Química, Universidad Nacional del Litoral, Santa Fe, Argentina
3 Campus Sete Lagoas, Universidade Federal de São João del-Rei, Sete Lagoas, Brazil



Yoghurt + *B. longum* 51A

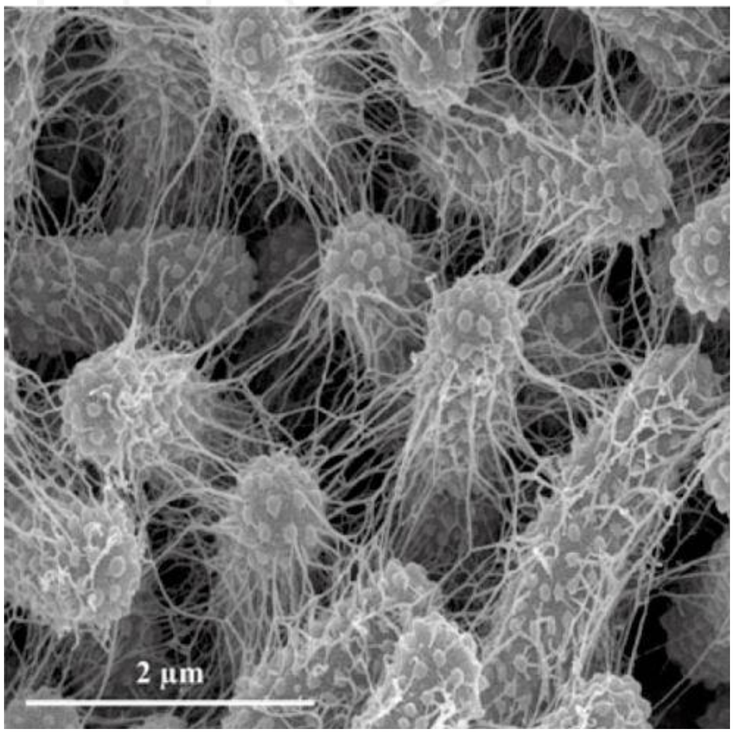
***Bifidobacterium longum* 51A**

Yoghurt

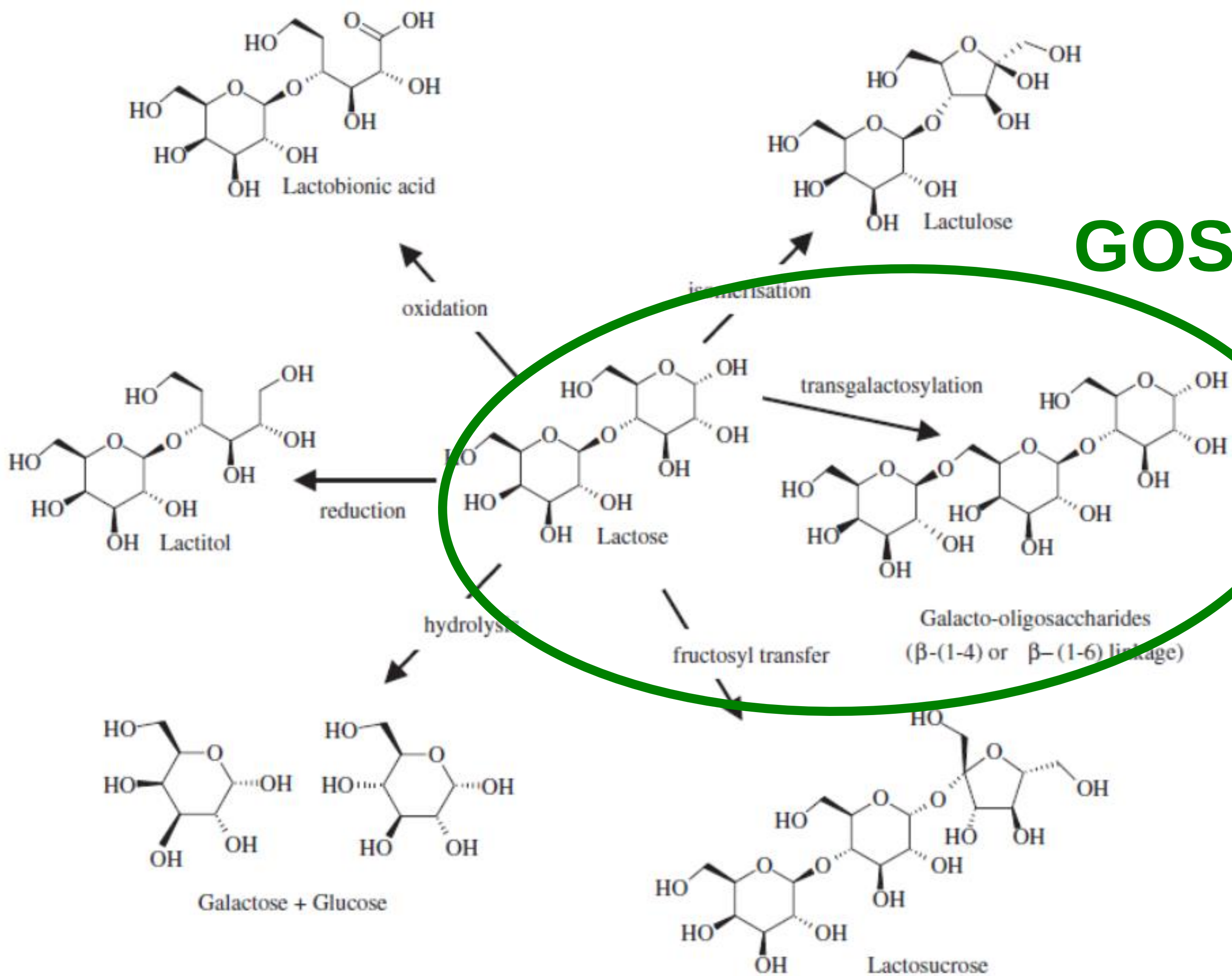
Control

Exopolysaccharides of Lactic Acid Bacteria for Food and Colon Health Applications

Tsuda Harutoshi



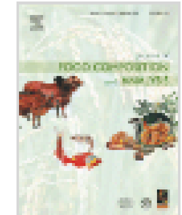
Trans-galactosilation during fermentation



ELSEVIER

Journal of Food Composition and Analysis

Volume 21, Issue 7, November 2008, Pages 540–544



Original Article

Study of galactooligosaccharide composition in commercial fermented milks

Cristina Martínez-Villaluenga, Alejandra Cardelle-Cobas, Nieves Corzo, Agustín Olano

Show more

Commercial yogurts containing bifidobacteria showed higher amounts of GOS (0.36–0.58%) than ready-to-drink yogurts containing *L. casei* (0.29–0.44%) and **traditional yogurts** (0.22–0.25%). Since GOS are recognised as prebiotic, information about their content in fermented milks would help to estimate the potential prebiotic activity of commercial products manufactured under different conditions.

Understanding Metchnikoff to the light of the knowledge today

(NGS, metagenomics).

Beneficial Microbes, 2016; 7(4): 473-484

Wageningen Academic Publishers

Effect of probiotic yoghurt on animal-based diet-induced change in gut microbiota: an open, randomised, parallel-group study

T. Odamaki[1*], K. Kato[1], H. Sugahara[1], J.Z. Xiao[1], F. Abe[1] and Y. Benno[2]

[1]*Food Science and Technology Institute, Morinaga Milk Industry Co., Ltd., 1-83, 5-chome, Higashihara, 252-8583 Zama-city, Kanagawa, Japan;* [2]*Benno Laboratory, Innovation Center, RIKEN, Wako, Japan; t-odamak@morinagamilk.co.jp*

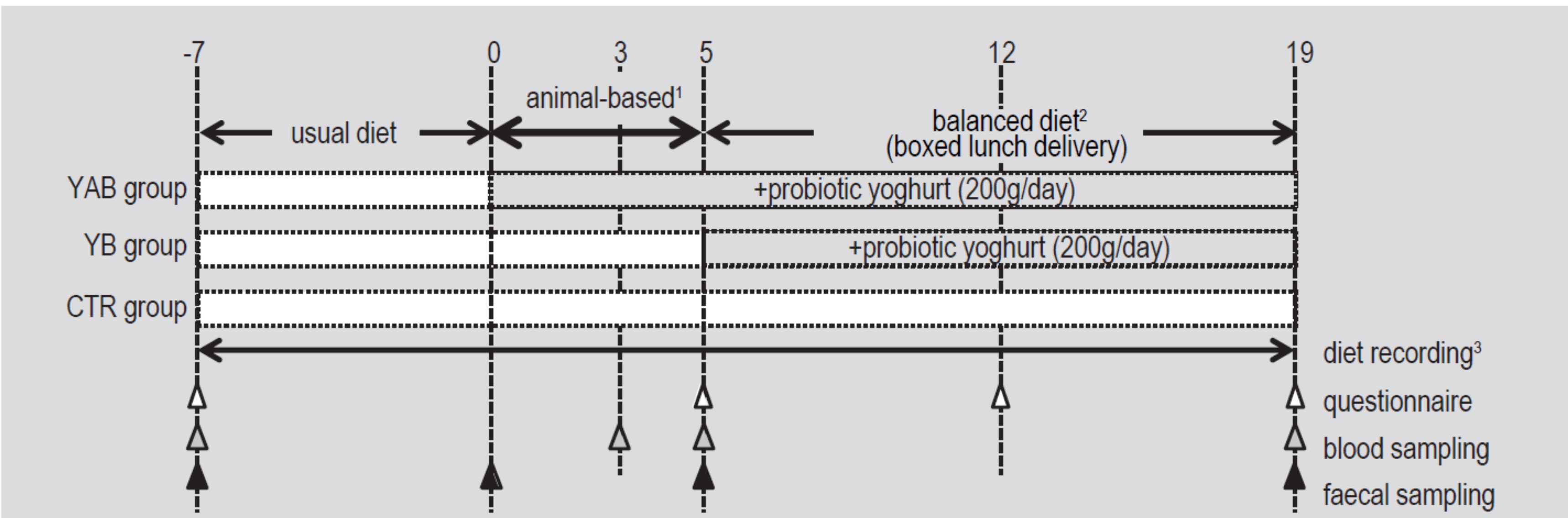
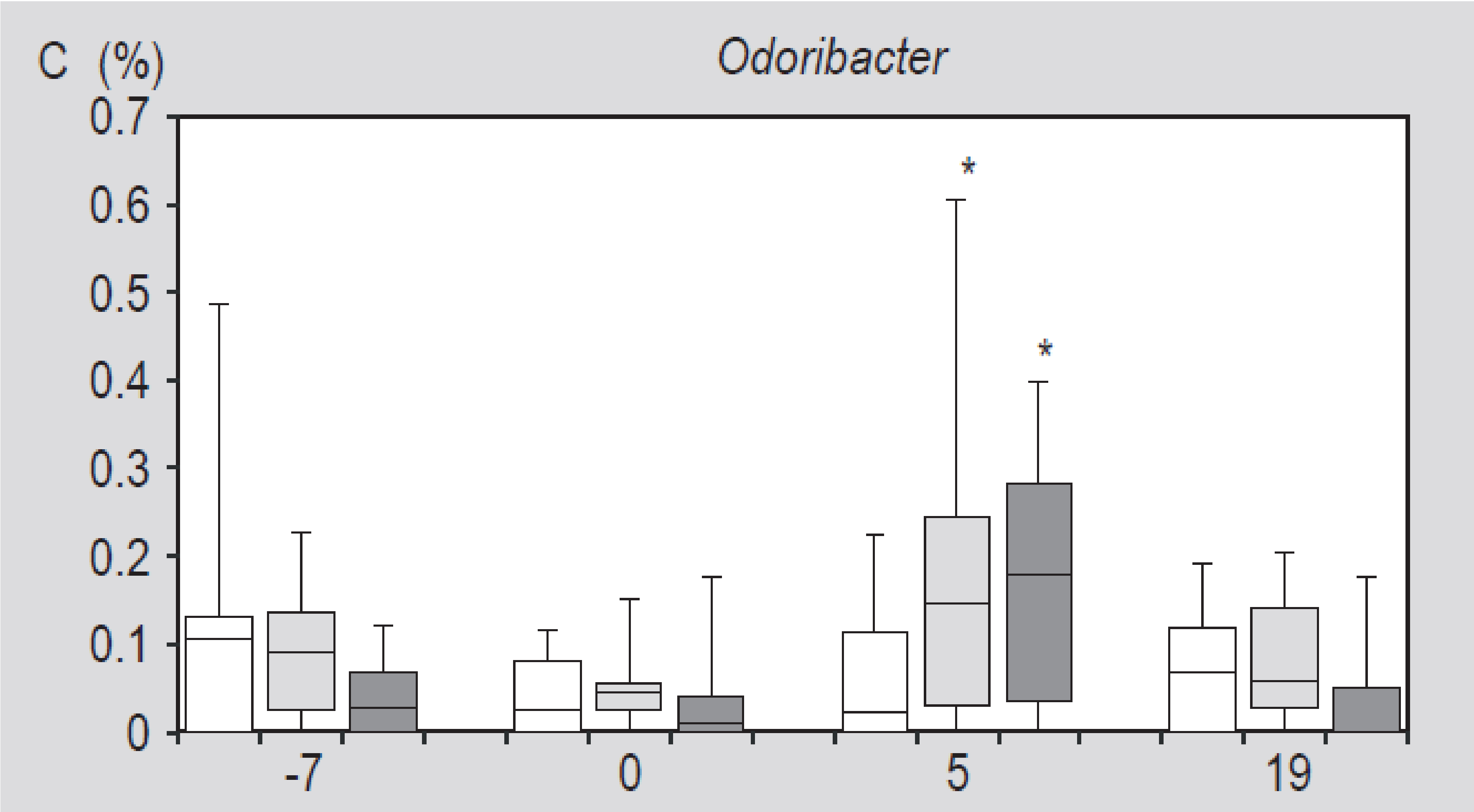


Figure 2. Schematic outline of the study design (YAB = subjects who ingested yoghurt during both the animal-based and balanced diet periods; YB = subjects who ingested yoghurt during the balanced diet period; CTR = control).[1] Composed of meat and egg (including processed foods, such as bacon and sausages). [2] Ingredients are provided in Supplementary Table S1. [3] Each diet was recorded by taking a photo and by answering a questionnaire.


C (%)
Odoribacter
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
*
*
-7
0
5
19

Brain, Behavior, and Immunity 65 (2017) 20–32

Revisiting Metchnikoff: Age-related alterations in microbiota-gut-brain axis in the mouse

Karen A. Scott [a], Masayuki Ida [b], Veronica L. Peterson [a,c], Jack A. Prenderville [a], Gerard M. Moloney [c], Takayuki Izumo [b], Kiera Murphy [d], Amy Murphy [d], R. Paul Ross [e], Catherine Stanton [d], Timothy G. Dinan [a,f], John F. Cryan [a,c,*]

[a] *APC Microbiome Institute, University College Cork, Cork, Ireland*
[b] *Suntory Wellness Limited, Suntory World Research Centre, Kyoto, Japan*
[c] *Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland*
[d] *Teagasc Moorepark Food Research Centre, Fermoy, Co. Cork, Ireland*
[e] *Department of Science, Engineering and Food Science, University College Cork, Cork, Ireland*
[f] *Department of Psychiatry & Neurobehavioural Science, University College Cork, Cork, Ireland*

A R T I

Article hist
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Keywords:
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Anxiety
Behaviour
Cognitive
Gut perme

Increaseof *Odoribacter* in aged-mice

Yoghurt ~~prevent aging~~ may delay aging of the microbiota.

clud- that y the rising n the rofile eases eased cyto- aecal genus ssoci- more, rders, was directly correlated with anxiety-like behaviour in aged mice. These changes suggest that changes in the gut microbiota and associated increases in gut permeability and peripheral inflammation may be important mediators of the impairments in behavioural, affective and cognitive functions seen in ageing.

Are probiotics worth from an economical point of view?

The cost-benefit issue

Infect Control Hosp Epidemiol. 2016 Sep;37(9):1079-86. doi: 10.1017/ice.2016.134. Epub 2016 Jul 5.

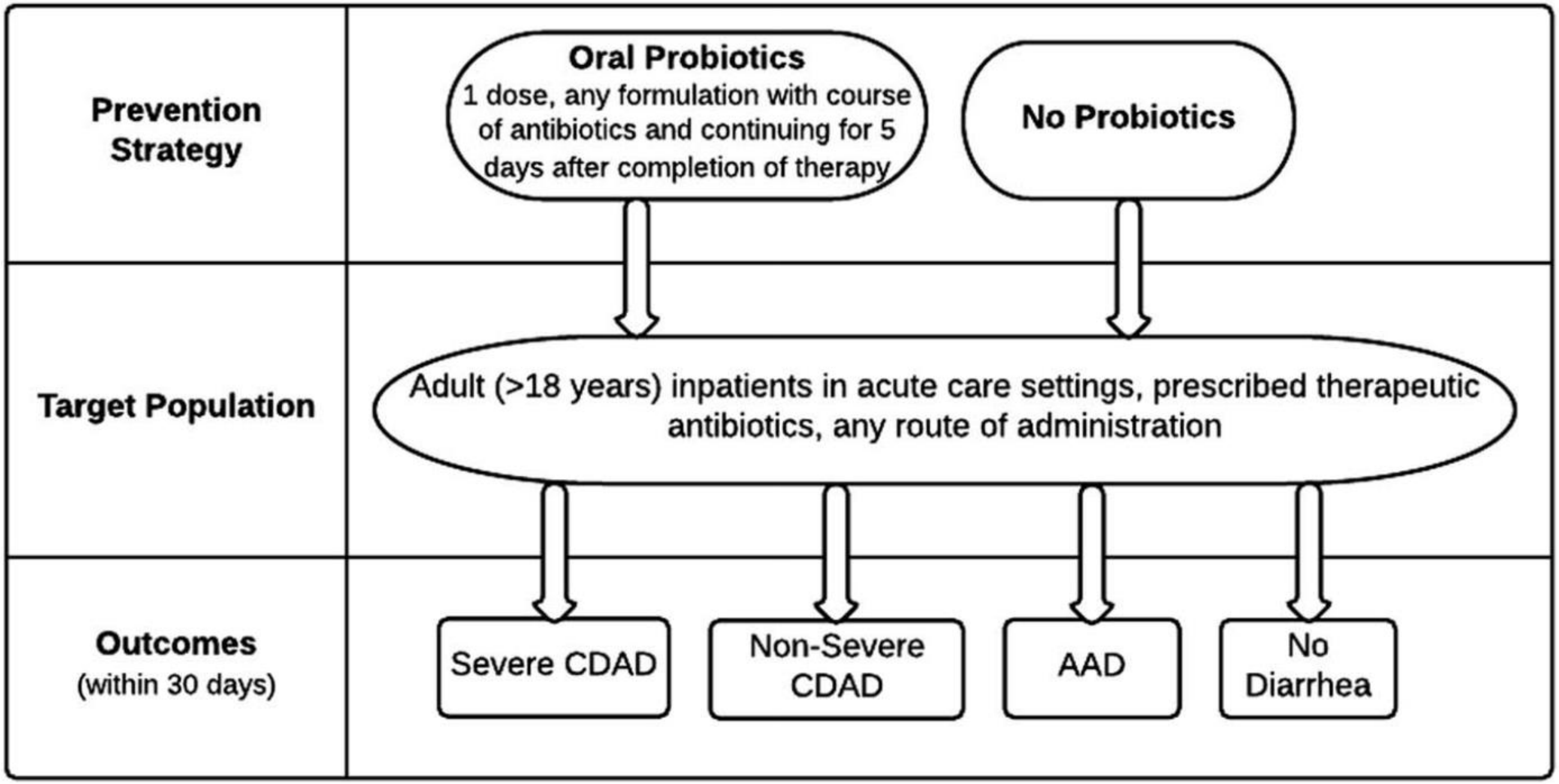
Cost-Effectiveness Analysis of the Use of Probiotics for the Prevention of Clostridium difficile-Associated Diarrhea in a Provincial Healthcare System.

Leal JR[1], Heitman SJ[2], Conly JM[2], Henderson EA[1], Manns BJ[3].

Author information

Abstract

OBJECTIVE To conduct a full economic evaluation assessing the costs and consequences related to probiotic use for the primary prevention of Clostridium difficile-associated diarrhea (CDAD). DESIGN Cost-effectiveness analysis using decision analytic modeling. METHODS A cost-effectiveness analysis was used to evaluate the risk of CDAD and the costs of receiving oral probiotics versus not over a time horizon of 30 days. The target population modeled was all adult inpatients receiving any therapeutic course of antibiotics from a publicly funded healthcare system perspective. Effectiveness estimates were based on a recent systematic review of probiotics for the primary prevention of CDAD. Additional estimates came from local data and the literature. Sensitivity analyses were conducted to assess how plausible changes in variables impacted the results. RESULTS Treatment with oral probiotics led to direct costs of CDN $24 per course of treatment per patient. On average, patients treated with oral probiotics had a lower overall cost compared with usual care (CDN $327 vs $845). The risk of CDAD was reduced from 5.5% in those not receiving oral probiotics to 2% in those receiving oral probiotics. These results were robust to plausible variation in all estimates. CONCLUSIONS Oral probiotics as a preventive strategy for CDAD resulted in a lower risk of CDAD as well as cost-savings. The cost-savings may be greater in other healthcare systems that experience a higher incidence and cost associated with CDAD. Infect Control Hosp Epidemiol 2016;37:1079-1086.



U$S 24/individual (30 days horizon), allowed U$S 518 saving/patient

frontiers in
PHARMACOLOGY

ORIGINAL RESEARCH ARTICLE
published: 17 February 2014
doi: 10.3389/fphar.2014.00013

Nutrition economic evaluation of a probiotic in the prevention of antibiotic-associated diarrhea

Irene Lenoir-Wijnkoop[1,2]*, Mark J. C. Nuijten[3], Joyce Craig[4] and Christopher C. Butler[5]

[1] Department of Pharmaceutical Sciences, University of Utrecht, Utrecht, Netherlands
[2] Scientific Affairs, Danone Research, Palaiseau, France
[3] Ars Accessus Medica, Amsterdam, Netherlands
[4] York Health Economics Consortium Limited, University of York, York, UK
[5] Institute of Primary Care and Public Health, School of Medicine, Cardiff University, Cardiff, UK

U$S 430 saving/patient

Edited by:
Dominique J. Dubois, Université Libre de Bruxelles, Belgium

Reviewed by:
Eric Claassen, Erasmus Medical Centre, Netherlands
John Hutton, University of York, UK

****Correspondence:***
Irene Lenoir-Wijnkoop, Department of Pharmaceutical Sciences, University of Utrecht, Universiteitsweg 99, 3584 CG Utrecht, Netherlands
e-mail: p.i.lenoir-wijnkoop@uu.nl

Introduction: Antibiotic-associated diarrhea (AAD) is common and frequently more severe in hospitalized elderly adults. It can lead to increased use of healthcare resources. We estimated the cost-effectiveness of a fermented milk (FM) with probiotic in preventing AAD and in particular *Clostridium difficile*-associated diarrhea (CDAD).

Methods: Clinical effectiveness data and cost information were incorporated in a model to estimate the cost impact of administering a FM containing the probiotic *Lactobacillus paracasei ssp paracasei* CNCM I-1518 in a hospital setting. Preventing AAD by the consumption of the probiotic was compared to no preventive strategy.

Results: The probiotic intervention to prevent AAD generated estimated mean cost savings of £339 per hospitalized patient over the age of 65 years and treated with antibiotics, compared to no preventive probiotic. Estimated cost savings were sensitive to variation in the incidence of AAD, and to the proportion of patients who develop non-severe/severe AAD. However, probiotics remained cost saving in all sensitivity analyses.

Conclusion: Use of the fermented dairy drink containing the probiotic *L. paracasei* CNCM I-1518 to prevent AAD in older hospitalized patients treated with antibiotics could lead to substantial cost savings.

Public Health and Budget Impact of Probiotics on Common Respiratory Tract Infections: A Modelling Study

Irene Lenoir-Wijnkoop[1,2]*, **Laetitia Gerlier**[3], **Jean-Louis Bresson**[4], **Claude Le Pen**[5], **Gilles Berdeaux**[3]¤

1 Utrecht University, Department of Pharmaceutical Sciences, Utrecht, The Netherlands, **2** Public Health & Scientific Relations, Danone Company, Paris, France, **3** IMS RWES HEOR, Vilvoorde, Belgium, **4** Université Descartes, Hôpital Necker-Enfants Malades, Paris, France, **5** Université Paris Dauphine, Paris, France

¤ Current Address: Conservatoire National des Arts et Métiers, Paris, France
* P.I.Lenoir-Wijnkoop@uu.nl

PLOS ONE | DOI:10.1371/journal.pone.0122765 April 10, 2015

Abstract

Objectives

Two recent meta-analyses by the York Health Economics Consortium (YHEC) and Cochrane demonstrated probiotic efficacy in reducing the duration and number of common respiratory tract infections (CRTI) and associated antibiotic prescriptions. A health-economic analysis was undertaken to estimate the public health and budget consequences of a generalized probiotic consumption in France.

Methods

A virtual age- and gender-standardized population was generated using a Markov microsimulation model. CRTI risk factors incorporated into this model were age, active/passive smoking and living in a community setting. Incidence rates and resource utilization were based on the 2011-2012 flu season and retrieved from the French GPs Sentinelles network. Results of both meta-analyses were independently applied to the French population to estimate CRTI events, assuming a generalized probiotic use compared to no probiotics during winter months: -0.77 days/CRTI episode (YHEC scenario) or odds-ratio 0.58 for $\geq$1 CRTI episode (Cochrane scenario) with vs. without probiotics. Economic perspectives were National Health System (NHS), society, family. Outcomes included cost savings related to the reduced numbers of CRTI episodes, days of illness, number of antibiotic courses, sick leave days, medical and indirect costs.

In France, the use of probiotics would avoid 2.4 millions of common **infections** of the respiratory tract, 291.000 doses of **atb** and 581,000 days of **absenteeism** from work. Saving 14.6 millions euros.

The Clinical and Economic Impact of Probiotics Consumption on Respiratory Tract Infections: Projections for Canada

Irene Lenoir-Wijnkoop[1,2]*, Laetitia Gerlier[3], Denis Roy[4], Gregor Reid[5]

1 Department of Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands, **2** Director Public Health &Scientific Relations, Danone Company, Paris, France, **3** QuintilesIMS Real-World Evidence, Zaventem, Belgium, **4** Department of Food Sciences, Laval University, Quebec, Canada, **5** Canadian Research and Development Centre for Probiotics, University of Western Ontario, London, Ontario, Canada

* P.I.Lenoir-Wijnkoop@uu.nl

Abstract

Introduction

There is accumulating evidence supporting the use of probiotics, which are defined as "live micro-organisms which, when administered in adequate amounts, confer a health benefit on the host", as a preventive measure against respiratory tract infections (RTI). Two recent meta-analyses showed probiotic consumption (daily intake of 10^7 to 10^{10} CFU in any form for up to 3 months) significantly reduced RTI duration, frequency, antibiotic use and work absenteeism.

Objectives

The aim of this study was to assess the impact of probiotic use in terms of number of RTI episodes and days averted, and the number of antibiotic prescriptions and missed workdays averted, in the general population of Canada. In addition, the corresponding economic impact from both a healthcare payer and a productivity perspective was estimated.

Methods

A microsimulation model was developed to reproduce the Canadian population (sample rate of 1/1000 = 35 540 individuals) employing age and gender. RTI incidence was taken from FluWatch consultation rates for influenza-like illness (2013–14) and StatCan all-cause consultations statistics. The model was calibrated on a 2.1% RTI annual incidence in the general population (5.2 million RTI days) and included known risk factors (smoking status, shared living conditions and vaccination status). RTI-related antibiotic prescriptions and work absenteeism were obtained from the literature.

In Canada, the use of probiotics would avoid 573,000 to 2.3 millions of common **infections** of the respiratory tract, 52,000 to 84,000 doses of **atb** and 330,000 to 500,000 days of **absenteeism** from work. Saving 1.3 to 8.9 millions eurosin Public Health and 61.2 to 99.7 millions euros in the Private Sector.

Osteoporos Int (2013) 24:139–150
DOI 10.1007/s00198-012-1998-6

ORIGINAL ARTICLE

Dairy foods and osteoporosis: an example of assessing the health-economic impact of food products

F. J. B. Lötters · I. Lenoir-Wijnkoop · P. Fardellone · R. Rizzoli · E. Rocher · M. J. Poley

Received: 29 January 2012 / Accepted: 3 April 2012 / Published online: 16 June 2012

Abstract
Summary Osteoporosis has become a major health concern, carrying a substantial burden in terms of health outcomes and costs. We constructed a model to quantify the potential effect of an additional intake of calcium from dairy foods on the risk of osteoporotic fracture, taking a health economics perspective.

Introduction This study seeks, first, to estimate the impact of an increased dairy consumption on reducing the burden of osteoporosis in terms of health outcomes and costs, and, second, to contribute to a generic methodology for assessing the health-economic outcomes of food products.
Methods We constructed a model that generated the number of hip fractures that potentially can be prevented with dairy foods intakes, and then calculated costs avoided, considering the healthcare costs of hip fractures and the costs of additional dairy foods, as well as the number of

F. J. B. Lötters
Institute of Health Policy and Management (iBMG),

Abstract

Summary Osteoporosis has become a major health concern, carrying a substantial burden in terms of health outcomes and costs. We constructed a model to quantify the potential

Introduction This study seeks, first, to estimate the impact of an increased dairy consumption on reducing the burden of osteoporosis in terms of health outcomes and costs, and, second, to contribute to a generic methodology for assessing

Nutri-economy

Potential economical and nutritional impact of the intake of dairy products.

N° of hip fractures that could be avoided every year:

2023 in France, 129 millions euros
455 in Sweden, 34 millions euros
132 in Holland, 6 millions euros

Amiens, France

R. Rizzoli
University Hospital Geneva, Bone Diseases,
Geneva, Switzerland

of nutrition and health economics. Future research should further collect longitudinal population data for documenting the net benefits of increasing dairy consumption on bone health and on the related utilization of healthcare resources.

Take-home messages…

1) We, *Homo sapiens,* have been living in contact with live bacteria (mainly through food) for more than 99% of our existence.
2) The loss of contact (C-section, reduced lactation, excessive atb and sanitization, western diet) led to an increase of autoimmune and inflammatory diseases.
3) We need microbes to educate our immune system and to keeping it working.
4) Yoghurt is one of the very few foods that are healthy and that can provide large amount of friendly bacteria at the same time.
5) Fermentation changes milk composition for good. New metabolites appear.
6) Probiotics can enhance the health impact of yoghurt itself.
7) Dairy products and probiotics may have a significant impact in saving money in Public Health and in the Private Sector.

Thank you !

Fermentation, fermented products and probiotics

Dr. Gabriel Vinderola

Investigador Independiente CONICET
Instituto de Lactología Industrial (INLAIN, UNL-CONICET)
Profesor Asociado, Cátedra de Microbiología
Departamento de Ingeniería de Alimentos
Facultad de Ingeniería Química
Universidad Nacional del Litoral, Santa Fe
gvinde@fiq.unl.edu.ar

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