
ANTIBIOTICS - TO TAKE OR NOT TO TAKE?

That is the question. Here is the answer.



Here for you before, during and after antibiotics.



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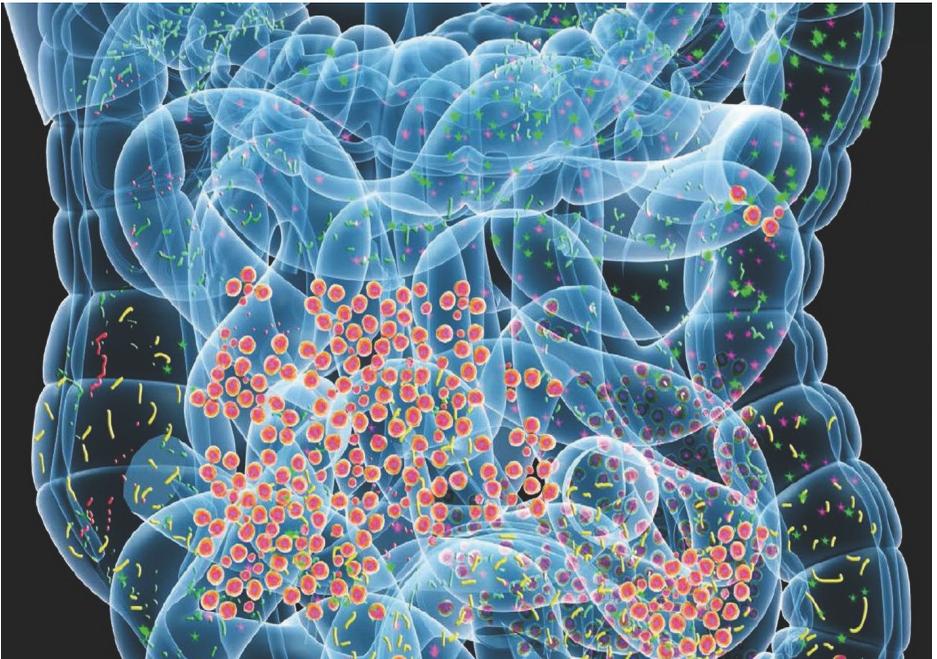
Friends in Our Gut

A fundamental idea about health and medicine has changed dramatically these past 30 years. That idea is the important role played by bacteria in keeping us healthy.

Ask people if bacteria are bad for us and most will say, “Yes”. Ask again if our immune system should kill bacteria to protect us from falling sick and the answer will usually be, “Yes” too.

But no, what was assumed to be “fact” is now known to be wrong. Very wrong. Clinical and scientific research has repeatedly turned our previous understanding of how germs are linked to our immunity, health and disease upside down! Germs such as bacteria are not bad for health. They are good - in fact essential - to health!

A healthy human being has 100 million million bacteria in our gut. There are over 10 times more bacteria co-existing with us than there are human cells. It may even be said that we are actually more bacterial than we are human! These good bacteria form a microbial community in our intestinal tract called our “microbiota” and sustain an ecological system within our bodies called our “microbiome”.



Why Has Mankind Evolved in Harmony with Bacteria?

Scientific research over the past two decades has revealed that our microbiota is essential to most of our bodily functions.¹

Since our intestinal tract contains nearly 75% of all our immune cells, the presence of a healthy microbiome determines how our immune system develops and functions. The good bacteria play a central role in educating, maturing and balancing our immune system so that our immunity is kept activated, yet under control. Our bacteria play a vital part in keeping our immune system in check.²

These bacteria reduce inflammation in the intestines and liver.^{2 3 4} They promote and coordinate the growth and repair of the cells in our gastro-intestinal tract⁴ and protects us from invasions by bad germs.⁵ Our microbiota influences how fat or thin we are⁶, how blood sugar is handled⁷, protects us from toxins⁸ and influences how we process food and medicines.⁹ It impacts on whether we become allergic or not.^{10 11} It influences the ageing process.¹² It even affects brain development¹³ and what our mood is!^{14 15}

What Can Disrupt Our Precious Microbiota?

Now that we know how important our microbiota is, what can destroy our microbiota and upset its natural composition? The single most powerful instrument of destruction of the microbiota is antibiotics.

There are two consequences when antibiotics are used.



Short term use of antibiotics

Most antibiotics destroy bacteria indiscriminately, taking out our good bacteria as well as the bad ones. It has been found that taking a course of antibiotic can disrupt the bacterial number, composition and balance for long periods, even up to a month.

One consequence of destruction of our protective gut microbiota is the invasion of harmful microorganisms. These bad germs are usually kept away by our intact microbiota but will find the chance to overwhelm the body's defences when the microbiota is disrupted by antibiotics. These unwelcome newcomers can cause gastro-intestinal upset known as antibiotic-associated diarrhoea in 5-30% of

patients.¹⁶ Antibiotic-associated diarrhoea may cause the patient to interrupt, abandon or change the course of antibiotics, resulting in treatment failure.

In the worst situation a super bad bacterium called *Clostridium difficile*, can establish itself in the intestinal tract, where it can remain long term, causing non-stop, or even life-threatening diarrhoea.



Long term overuse or misuse of antibiotics - Too much of a good thing

Overuse of antibiotics produces drastic changes in a person's microbial ecosystem, disrupting the intestinal microbiome of not only the individual taking antibiotics^{17 18 19} but also in the microbial ecosystem of the community.²⁰

Destruction of the microbiome results in disruption of a person's immunity, making the person less able to fight infections.²¹

Worse, when antibiotics are used repeatedly long term, bad bacteria can mutate into stronger and stronger bacteria as they try to fight off the antibiotics. This results in infections which are increasingly difficult to treat or the outbreak of infection by "superbugs". Superbugs come about because prolonged or overuse of antibiotics in a community selects out bacteria which become more and more resistant to the antibiotics used in that community.

Since Sir Alexander Fleming discovered penicillin in 1928, antibiotics have saved countless lives. Antibiotics are one of mankind's wonder drugs. It is because antibiotics are so important and so useful that we must make sure we can still

continue to have effective antibiotics to fight bad bacteria whenever the need arises.

Unfortunately, antibiotics have been so greatly misused and overused by humans and animals that antibiotics are rapidly losing their effectiveness.

The increasing emergence of “superbugs” in the past 2 decades has triggered alarm all over the world. These “superbugs” cannot be killed by many or even all available antibiotics.

Scientists just cannot produce anymore new or stronger antibiotics to kill more and more superbugs. Since the 1980s despite intensive scientific research, no new type of antibiotics has been discovered!²²



Alarming Overuse and Misuse of Antibiotics and Antibiotic-Pollution

The overuse and misuse of antibiotics cause overflow of antibiotics into the environment, contaminating sewage, soil and waters.^{23 24} Antibiotic pollution creates a breeding ground for the emergence of superbugs in the community.

Nowhere is it more alarmingly than in China.

Researchers in the Chinese Academy of Sciences in Guangzhou surveyed the use of antibiotics nationally in 2013.²⁴ They reported that China produced and used the most amount of antibiotics in the world – 162,000 tons of human and veterinary antibiotics with China’s eastern provinces consuming the maximum number of doses. The rate of use of antibiotics was 157 doses per day per 1000 persons meaning that China used at least 204 million doses of antibiotics everyday in contrast to the six times lower amount used per day in UK and the US! (Figure 1)

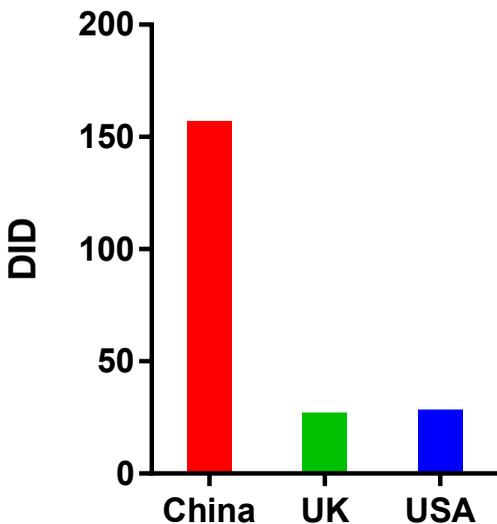


Figure 1: **Daily Antibiotic Use in China, UK and US.** *DID = Daily doses for 1000 Inhabitants per Day. Figure is modified from Ying et al. 2017.

Such inappropriate and extensive use of antibiotics in humans and livestock has resulted in widespread “antibiotic pollution” of the environment and food chain, threatening human health and the environment.

This serious public health risk was directly related to the degree of antibiotic-pollution in the environment such as in China’s river basins.^{24 25} Massive degree of antibiotic overuse has resulted in severe antibiotic pollution of waterways and river basins, especially so in the Pearl River Delta and the areas around Beijing. (Figure 2).

The researchers clearly demonstrated that the rate of bacterial resistance to antibiotics was directly related to the degree of environmental concentrations of antibiotics in the community.

Widespread use of antibiotics in man and animals was a major cause of a sharp rise in multi-drug resistant superbugs in China.^{25 26} Superbugs can rapidly spread throughout the country and to the rest of the world. The DNA of superbugs has even been isolated in the seawaters surrounding China²⁷ and in its air pollutants!²⁸

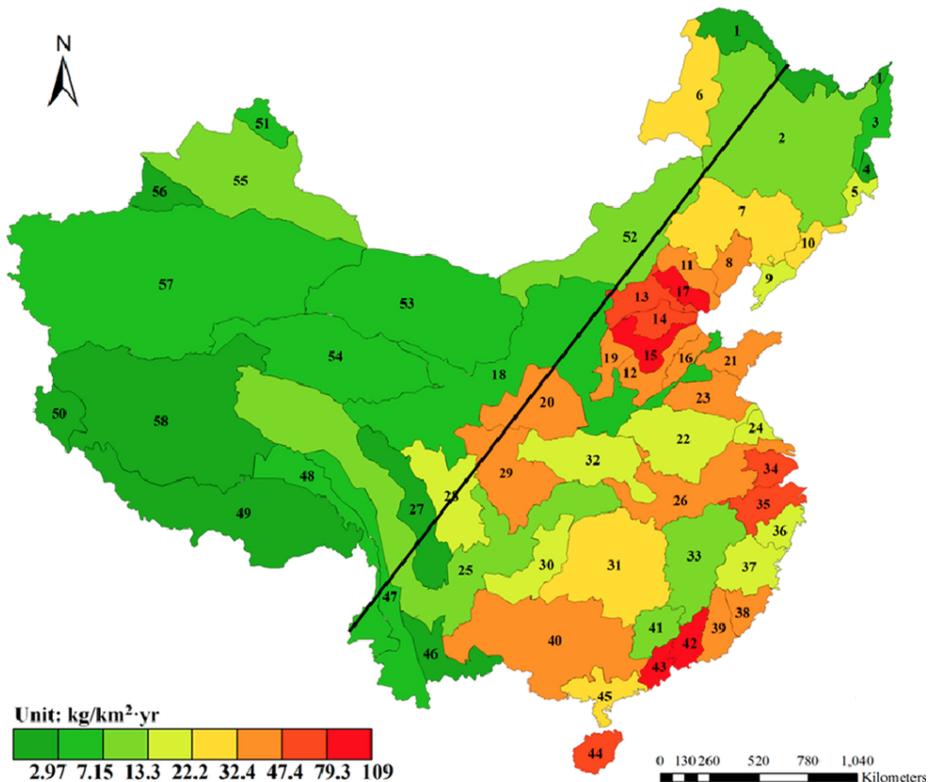


Figure 2: **Map of Antibiotic Pollution In China.**

Map shows the amounts of antibiotics polluting river basins of China.

Areas of interest: (13), (14), (15) and (17) = Beijing and surrounding areas
 (43) = Pearl River Delta.

Map adapted from Zhang et al. 2015.

What Can We Do to Save the Situation?

As an individual or a parent, you can do something.

1

Infants should be breastfed as far as possible. Breast fed babies have stronger immunity.

2

Take an antibiotic only when necessary.

3

Take antibiotics only for bacterial infections, not infections caused by viruses and fungi.

4

Never buy antibiotics off the shelf without first consulting your doctor.

5

Take antibiotics in the correct dose and timing and finish the course prescribed by your doctor. Not following the correct schedule and length of treatment can result in treatment failure, resulting in the need for further courses of antibiotics and the emergence of antibiotic-resistant bad germs.

6

As far as possible take an antibiotic which is designed to kill the specific type of bad germs which are making you ill, not one which is designed to kill a wide range of germs.

7

Take a probiotic bacterium in large enough numbers to supplement your microbiota before, during and after antibiotics.

8

Take a probiotic which has research showing it can reduce antibiotics' damage to the microbiome and immunity.

9

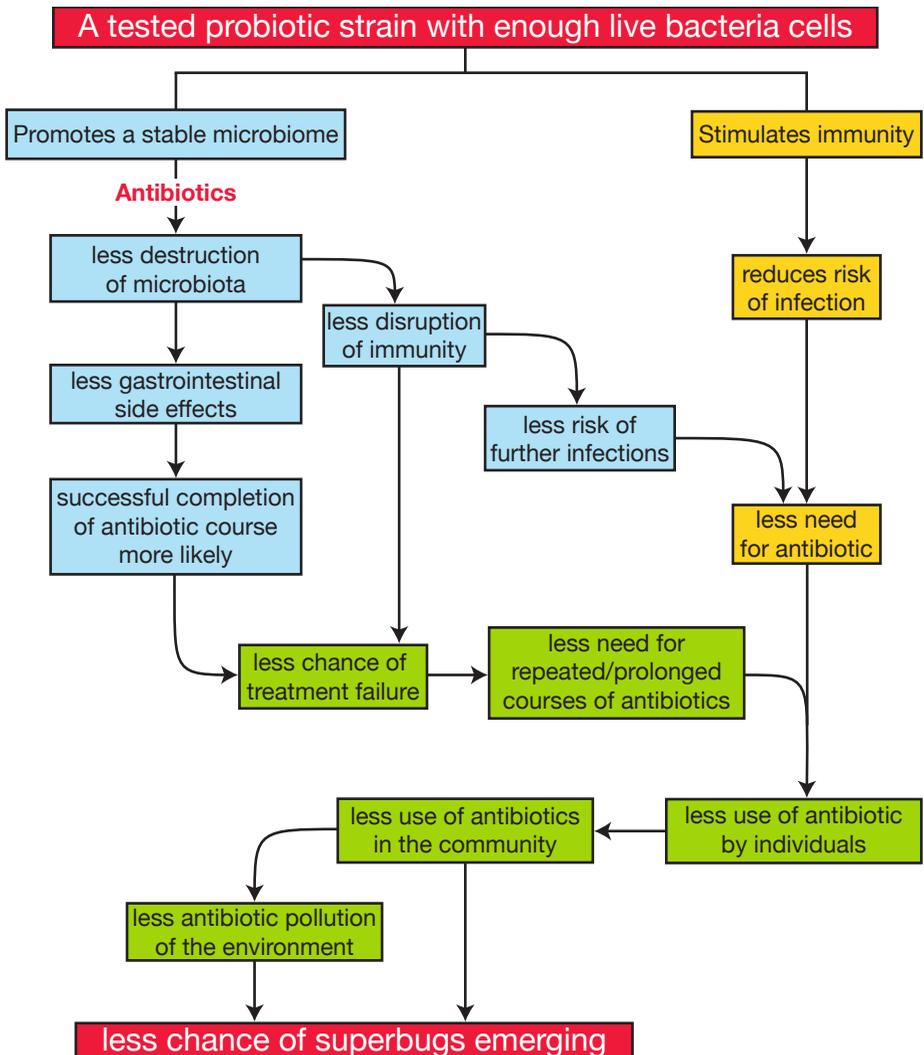
Take a probiotic which has been shown to stimulate immunity and reduce the need for antibiotics.

How Can a Probiotic Help to Reduce the Need for Antibiotics?

For a probiotic to be truly useful in reducing the negative health and environmental impact of antibiotics it should have the following beneficial actions:

- Stimulates immunity
- Reduces antibiotic-associated diarrhoea
- Reduces disruption of gut microbiota by antibiotics

How such a probiotic works is outlined below:-



Which Probiotic Can Do This?

In countries such as Japan, it is well-accepted practice that anyone who is prescribed an antibiotic should routinely consume probiotics.²⁹

But every probiotic is unique. Not every probiotic can do all of the above beneficial actions.

The World Health Organisation (WHO) and the Food and Agriculture Organisation have defined true probiotics as **only LIVE microorganisms which are consumed in LARGE ENOUGH numbers in order to produce beneficial effects.**³⁰

Yoghurt starters are not probiotics. And most bacteria sold as probiotics may be killed when taken with antibiotics.³¹

One strain which has research studies showing that it has all the above useful effects and can survive during a course of antibiotics is *Lactobacillus rhamnosus* GG (ATCC 53103) or the L. GG strain.^{32 33 34 35} This “GG” strain has over 1000 scientific research papers and more than 200 clinical studies.



The number of live probiotic bacteria which clinical studies have found to be most effective to produce the above beneficial effects is at least 10 to 20 billion in children and 20 billion in adults.^{32 33 34 35 36 37 38 39 40 41}

For best effect, it is preferred to separate a dose of antibiotic from the GG probiotic by 1-2 hours.

- A clinical study was conducted in Europe to test the effect of long term consumption of the “GG” probiotic in children on the side-effects of antibiotics as well as the composition of intestinal microbiota before and after the use of antibiotics.⁴²

The children took the probiotic everyday for 7 months and were continued to be observed for nearly 3 years afterwards.

The researchers found that long term daily “GG” consumption increased the composition of good bacteria in the gut. When the supplemented children took antibiotics they experienced less gastrointestinal side-effects. Taking the “GG” probiotic also protected the microbiota from being disrupted, even when penicillin was prescribed and at the same time, reduced the number of harmful intestinal bacteria.

Even more remarkable was the finding that during the nearly 3-year period following the use of probiotics and antibiotics the “GG” children took LESS antibiotics compared to the children who were never supplemented with the probiotic. This clinical study showed that children who took “GG” probiotic long term either experienced less infections or were more able to fight off infections without the need for antibiotics. The possible reason for reduced need for antibiotics in the “GG” group was that the probiotic prevented antibiotic-associated changes to the microbiota and thus maintained strong immunity.

This observed long-term protection against certain infections is a very valuable, beneficial effect which can help reduce the overuse of antibiotic. Without the need for repeated or further use of antibiotics, the severity of antibiotic pollution in our community will be reduced too.

- In 2014, a team of doctors in Queen Mary Hospital in Hong Kong, SAR China reported success in permanently clearing the superbug called “VRE” from patients after antibiotics when they were given 20 billion live “GG” probiotic bacteria a day for several months to rebuild the patients’ microbiome.⁴¹

How to Take The “GG” Probiotic?

The “GG” probiotic is contained in LACTOGG’s family of products*. There are high enough bacteria in the LACTOGG products to colonise the intestinal tract and produce beneficial effects. LACTOGG contains at least 20 billion live bacteria per capsule while LACTOGG+ contains at least 15 billion live bacteria in each drink sachet.

(*Not all the branded products may be available at the same time in individual countries.)

As demonstrated in clinical studies, this probiotic should be taken before, during and after antibiotics.

- “Before”** to stimulate immunity and give the body a chance to overcome infection without the need for antibiotics.
- “During”** to reduce the nasty side-effects of antibiotics.
- “After”** to build back the microbial eco-system and ensure immunity is regained.

Time for Action!

It is time for everyone to answer to the urgent call of global health agencies such as the WHO⁴³ and play a part in government initiatives⁴⁴, to protect ourselves from unnecessary antibiotics and antibiotic pollution. By working together we can ensure that one of mankind’s most valuable, life-saving treatments will continue to be effective when needed.

Instead of ANTibiotics, we should make use of specific PRObiotics with documented benefits.

Humans need good bacteria. **Keep our bacteria alive and happy and our bacteria will keep us healthy!**



LACTOGG. Here for you before, during and after antibiotics.

References / 参考

1. Marchesi JR et al. The gut microbiota and host health: a new clinical frontier. *Gut* 2016;65:330-9
2. Rook GAW and Burnet LR. Microbes, immunoregulation, and the gut. *Gut* 2005;54:317-320
3. Quigley EMM et al. The gut microbiota and the liver. Pathophysiological and clinical implications. *J Hepatic* 20-13;58:1020-7
4. Nowarski R et al. The stromal intervention: Regulation of immunity and inflammation at the epithelial-mesenchymal barrier. *Cell* 2017;168:362-375
5. Buffle CG et al. Microbiota-mediated colonization resistance against intestinal pathogens. *Nat Rev Immunol* 2013;13:790-801
6. Turnbaugh PJ and Gordon JL. The core gut microbiome, energy balance and obesity. *J Physiol* 2009;587:4153-8
7. Larsen N et al. Gut microbiota in human adults with Type 2 diabetes differs from non-diabetic adults. *PLoS ONE* 2010;5:e9085
8. Claus SP et al. The gut microbiota: a major player in the toxicity of environmental pollutants? *Biofilms Microbiomes* 2016;
9. Greenville C. Anti-cancer therapies affected by gut microbiota. *Nat Rev Gastroenterol Hepatol* 2014;11:1
10. Nyland L et al. Microarray analysis reveals marked intestinal microbiota aberrancy in infants having eczema compared to healthy children in at-risk for atopic disease. *BMC Microbiol* 2013;13:12 doi:10.1186/1471-2180-13-12
11. Abrahamsson T et al. Low gut microbiota diversity in early infancy precedes asthma at school age. *Clin Exp Allergy* 2014;44(6):842-850
12. Vaiserman AM et al - Gut microbiota: A player in aging and a target for anti-ageing intervention. *Ageing Res Rev* 2017;35:36-45
13. Mohle L et al. Ly6C^{hi} monocytes provide a link between antibiotic-induced changes in gut microbiota and adult hippocampal neurogenesis. *Cell Rep* 2016;15:1945-56
14. Petra AI et al. Gut-microbiota-brain axis and effect on neuropsychiatric disorders with suspected immune dysregulation. *Clin Ther* 2015;37(5):984-995
15. Foster JA et al. Gut-brain axis: how the microbiome influences anxiety and depression. *Trends Neurosci* 2013; 36:305-12
16. MacFarland LV et al. Epidemiology, risk factors and treatments for antibiotic-associated diarrhea. *Dig Dis* 1998;16:292-307
17. Korpela K et al. Intestinal microbiome is related to lifetime antibiotic use in Finnish pre-school children. *Nat Commun* 2016;7:10410. doi: 10.1038/ncomms10410
18. Dethlefsen L et al. Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation. *Proc Natl Acad Sci USA* 108:4554-61
19. Yassour M et al. Natural history of the infant gut microbiome and impact of antibiotic treatment on bacterial strain diversity and stability. *Sci Transl Med* 2016;8(343):343ra81. doi: 10.1126/scitranslmed.aad0917
20. Antonopoulos DA et al. Reproducible community dynamics of the gastrointestinal microbiota following antibiotic perturbation. *Infect Immun* 2009;77:2367-75
21. Brandl K et al. Vancomycin-resistant enterococci exploit antibiotic-induced immune deficits. *Nature* 2008;455(7214):804-7
22. Silver LL. Challenges of antibacterial discovery. *Clin Microbiol Rev*, 2011, 24(1):71-109. doi:10.1128/CMR.00030-10.
23. Huang Y et al. Simultaneous extraction of four classes of antibiotics in soil, manure and sewage sludge and analysis by liquid chromatography-tandem mass spectrometry with the isotope-labelled internal standard method. *Anal Methods* 2013;5:3721
24. Zhang Q-Q et al. Comprehensive evaluation of antibiotics emission and fate in the river basins of China: Source analysis, multimedia modelling, and linkage to bacterial resistance. *Environ Sci Technol* 2015;49:6772-82
25. Ying G-G et al. China must reduce its antibiotic use. *Environ Sci Technol* 2017;51:1072-3
26. Tang Q et al. Control of antibiotic resistance in China must not be delayed: the current state of resistance and policy suggestions for the government, medical facilities, and patients. *BioScience Trends* 2016;10(1):1-6
27. Zhu Y-G et al. Continental-scale pollution of estuaries with antibiotic resistance genes. *Nat Microbiol* 2017;2:16270
28. Pal C et al. The structure and diversity of human, animal and environmental resistomes. *Microbiome* 2016;4:54
29. Amagase H et al. Current marketplace for probiotics: a Japanese perspective. *Clin Infect Dis* 2008; 46(Suppl.):S73-S75
30. Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria, 2001
31. Hammed AM et al. Towards a compatible probiotic-antibiotic combination therapy: assessment of antimicrobial resistance in the Japanese probiotics. *J Appl Microbiol* 2010;109:1349-60
32. Goldin BR et al. Survival of Lactobacillus species (strain GG) in human gastrointestinal tract. *Dig Dis Sci* 1992;37:121-8
33. Arvola T et al. Prophyllactic Lactobacillus GG reduces antibiotic-associated diarrhoea in children with respiratory infections: a randomized study. *Pediatrics* 1999;104(5):e64
34. Vanderhoof JA et al. Lactobacillus GG in the prevention of antibiotic-associated diarrhoea in children. *J Pediatr* 1999;135:564-8
35. Armuzzi A et al. The effect of oral administration of Lactobacillus GG on antibiotic-associated gastrointestinal side-effects during Helicobacter pylori eradication therapy. *Aliment Pharmacol Ther* 2001;15:163-9
36. Saxelin M et al. Fecal recovery following oral administration of Lactobacillus strain GG(ATCC 53103) in gelatine capsules to healthy volunteers. *Int J Food Microbiol* 1995;25:199-203
37. Alander et al. Persistence of Colonization of Human Colonic Mucosa by a Probiotic Strain, Lactobacillus rhamnosus GG after Oral Consumption. *Appl Environ Microbiol* 1999; 65:351-4
38. Gorbach SL et al. Successful treatment of relapsing Clostridium difficile colitis with Lactobacillus GG. *Lancet* 1987 2:1519
39. Kukkonen K et al. Long-term safety and impact on infection rates of postnatal probiotic and prebiotic (synbiotic) treatment: randomised, double-blind, placebo-controlled trial. *Paediatrics* 2008;122:8-12
40. Sepp E et al. Effect of administration of Lactobacillus casei strain GG on the GI microbiota of newborns. *Microb Ecol Health Dis* 1993;6:309-14
41. Cheng VCC et al. Decolonization of gastrointestinal carriage of vancomycin-resistant Enterococcus faecium: case series and review of literature. *BMC Infect Dis* 2014;14:514. doi: 10.1186/1471-2334-14-514
42. Korpela K et al. Lactobacillus rhamnosus GG intake modifies preschool children's intestinal microbiota. alleviates penicillin-associated changes, and reduces antibiotic use. *PLoS ONE* 2016;11(4):e0154012
43. World Health Organisation. Antimicrobial Resistance Global Report on Surveillance 2014
44. National Action Plan to Contain Antimicrobial Resistance (2016-2020). http://en.nhfc.gov.cn/2016-08/26/c_70276.htm

