

Quick Facts

What is an FMT?

FMT (Faecal Microbiota Transplantation) uses normal 'healthy' human flora introduced into the patients bowel to 'kill' the bad bacteria. FMT therapy involves the infusion of healthy human donor flora bacteria into the bowel of the patient. The infusion is repeated for at least 5 days or longer. The therapy includes a special low fibre diet prior to infusion and a course of antibiotics to kill off as many bad bacteria as possible before infusion. Killing off 'bad' bacteria before infusion gives the newly introduced 'good' bacteria a better chance of re-establishing dominance. Preparation also includes a bowel washout prior to infusion.<sup>(6)</sup>

Study shows probiotics may help ease allergies

by Matt Batcheldor

(Vanderbilt University)<sup>(7)</sup> Using probiotics may help alleviate the symptoms of allergic rhinitis (AR), also known as seasonal or perennial allergies, according to a Vanderbilt study that reviewed 23 previous trials.

The results were published in April in the online version of the journal *International Forum of Allergy & Rhinology*.<sup>(8)</sup>



Justin Turner, M.D., Ph.D.

"When you look at all the studies combined, there was a statistically significant improvement in both the rhinitis-specific quality of life of those patients and in their nasal specific quality of life," said lead author Justin Turner, M.D., Ph.D., assistant professor of Otolaryngology. But he cautioned that "the jury is still out" and suggests the topic is ripe for future studies.

Probiotics are microorganisms that are thought to have gastrointestinal benefits when consumed.

They are present in some foods, such as yogurt, or can be taken as a dietary supplement. But comprehensive data about their effectiveness is more difficult to come by because they are regulated as a supplement and not as a drug, Turner said.

The study, which included Alexander Zajac, M.D. a resident in General Surgery and, Austin Adams, M.D., a resident in Otolaryngology Surgery, "represents the most comprehensive analysis to date on the use of probiotics for the treatment of AR," according to the journal article.

"It was a systematic review where basically we just searched the medical literature for all studies that have evaluated treatment of allergic rhinitis with probiotics," Turner said. "There was a lot of variability in the individual studies, but a majority of the studies did show at least some benefit with the use of probiotics compared to placebo."

Of the 23 studies that were reviewed, 17 showed that probiotics were linked to improvement in at least one facet of a patient's health - either rhinitis-specific quality of life or in symptoms. A total of 1,919 patients were involved.

"That means that six (studies) did not show any benefit at all, so it's hard to make any firm conclusions about that," Turner said. "We also found that the studies were very variable, so they used a lot of different bacterial strains and treatment durations."

Allergic rhinitis is a common disease that affects between 10 and 30 percent of the general population.

Turner cautioned that probiotics are not a substitute for current medications used to treat symptoms.

"This is not by any means suggesting that this is a cure for allergies," he said, but suggests that further studies on the topic are in order.



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Message from the Editor

15<sup>th</sup> Edition

Is there a role for probiotics in female vaginitis, allergic rhinitis and refractory Crohn's disease?

For those who like to know more, just spend a few precious minutes reading this newsletter and you will benefit from it.

Our editorial team would like to express our sincere appreciation to the contributors of this newsletter, and especially to Dr Chia Yin Nin for her insightful article.

God Bless !

Melvin Wong  
Editor-in-chief

Importance of Probiotics in Vagina Health

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Most women will experience one or more episodes of vaginal infection in their lifetime. Although seldom life-threatening (unless it is an STD e.g. gonorrhoea or syphilis), it is often irritating with distressing vulva itch and at times embarrassing with offensive discharge and odour.

Many factors can disrupt the normal flora of the vagina causing an infection to come on. Infections can be bacterial or fungal in nature. The 2 commonest vaginal infections are bacterial vaginosis and vulvovaginal candidiasis. To understand the cause of vaginal infection, we must first understand the normal healthy vagina.

The normal healthy vaginal pH is acidic 3.8-4.4. This acidic pH is important as it discourages infection from occurring. The acidic environment is created by normally occurring lactobacilli. There are many different strains of lactobacilli. The 2 commonest ones that inhabit the healthy vagina are Lactobacillus rhamnosus and Lactobacilli reuteri. The vaginal pH is also affected by hormones which fluctuate throughout the menstrual cycle, being least acidic on the days just prior to and during menstruations. This is also the time in the menstrual cycle whereby vaginal infections are the most common. The normal vagina is also colonised by pathological bacteria and fungus. Infections occur when such bacteria or fungus overgrow. Antibiotics usage especially broad-spectrum antibiotics e.g. Augmentin, often kills off both the pathological bacteria and the beneficial lactobacillus altering the vaginal pH predisposing one to vulvovaginal candidiasis. A weakened immune system due to chemotherapy or immunosuppressants can also increase one's

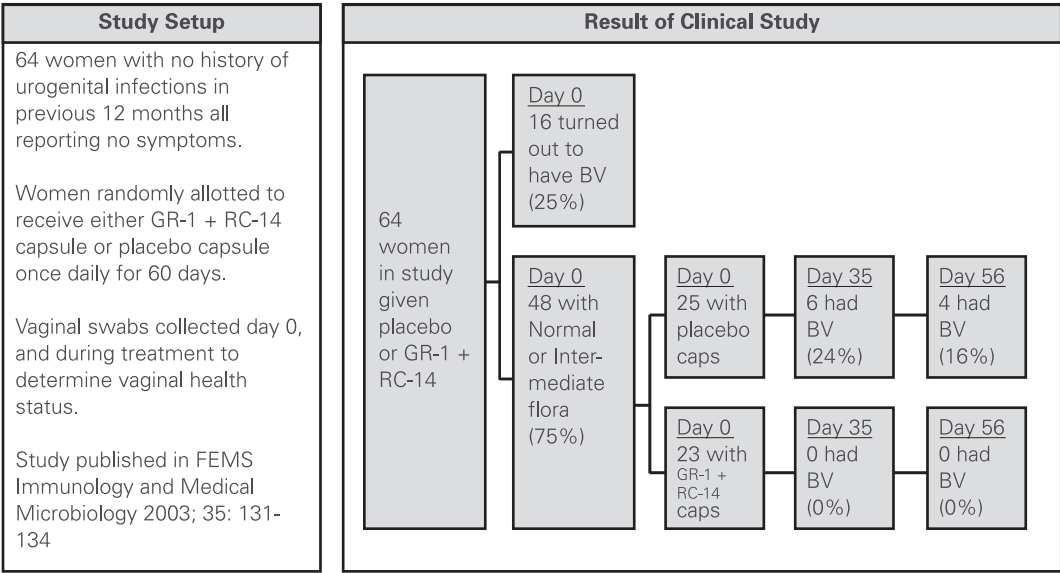


risk of vaginal infections. Diabetic patients are also at higher risks of vulvovaginal candidiasis. Other factors that can alter vaginal pH include semen and vaginal douching.

The good news is that incidence of vaginal infections can be reduced by maintaining a healthy vagina pH and flora. The easiest way is to ensure that there is sufficient lactobacillus in the vagina. Lactobacillus are normally

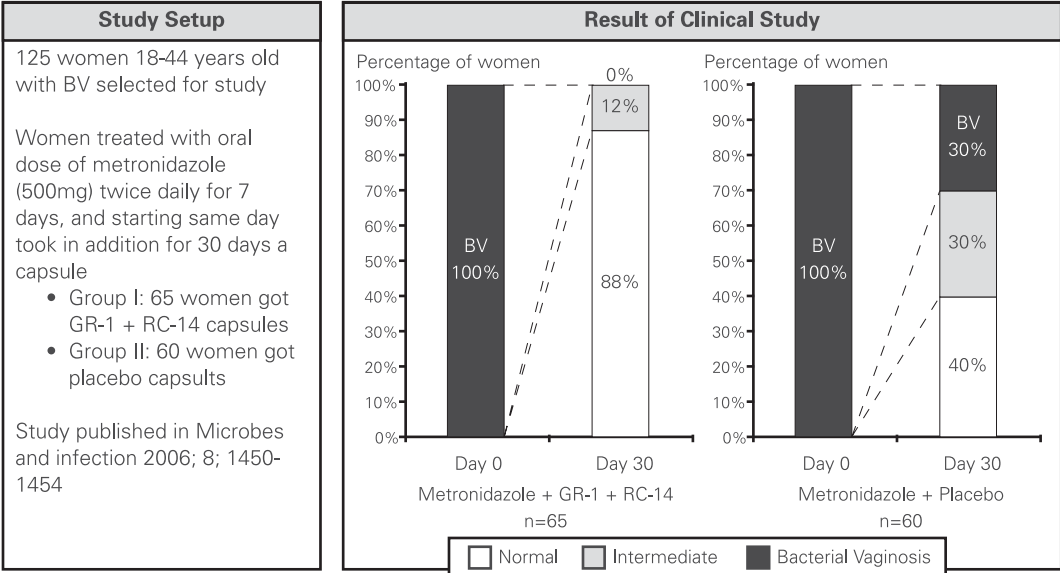
occurring in the vagina. They usually are acquired from food source and transmigrate from the intestinal tract to colonise the vagina. Probiotics supplementation is an easy and useful way to ensure sufficient intake of lactobacillus. Studies have shown that probiotics (GR1 + RC14) not only prevents bacterial vaginosis, vulvovaginal candidiasis in both healthy and at risks women (at risks defined as women who are diabetics, on immunosuppressants, antibiotic therapy, pregnant).

Lactobacillus rhamnosus ( GR-1 ) + Lactobacillus reuteri ( RC-14 ) prevents Bacterial Vaginosis (1)



Probiotics have also been shown to be more effective than antibiotics and antifungal alone in the treatment of bacterial vaginosis and vulvovaginal candidiasis.

GR-1 + RC-14 and antibiotics more effective than antibiotics alone (2)



GR-1 + RC-14 increases the effectiveness of an anti-fungal agent (fluconazole) in treatment of yeast vaginitis (3)

Design

- Randomized, double-blind, placebo-controller
- 55 women, 16-46 years of age, diagnosed with yeast vaginitis
- 2 capsules daily of 1 billion CFU each + single dose antifungal (fluconazole)
- 4 weeks duration
- Symptoms of yeast vaginitis was recorded; itching and burning vaginal feeling, pain at urination or sexual intercourse

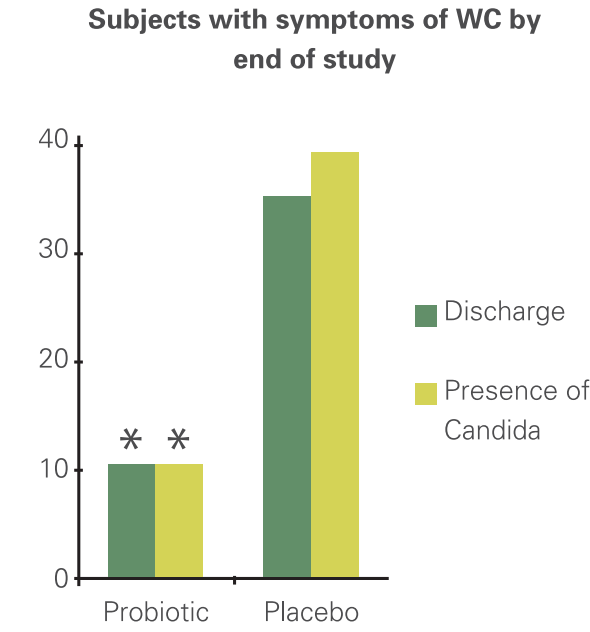
Results

- Probiotic group demonstrated reduction of discharge: 10.3% compared to 34.6% in placebo group (figure)
- Probiotic group demonstrated reduction in presence of Candida; 10.3% compared to 38.5% in placebo group (figure)

Conclusion

- The GR-1 + RC-14 concept can increase the effectiveness of an anti-fungal pharmaceutical agent in curing disease

In conclusion, probiotics are now recognized as important in maintaining good vaginal health and in preventing vaginal infections. It also helps in the treatment of



established infection increasing the cure rates as well as preventing the reoccurrence rates.

Dr. Faming Zhang, on treating refractory Crohn's disease with fecal microbiota transplantation

By Kristina Campbell, M.Sc.



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(GMFH)<sup>(4)</sup> Dr. Faming Zhang, MD, PhD, is a doctor and researcher at the Institute for Digestive Endoscopy & Medical Center for Digestive Diseases at The Second Affiliated Hospital of Nanjing Medical University in Nanjing, China. He is Vice Chief of the Medical Center for Digestive Diseases, and Director of Intestinal Diseases.

His research group recently published a pilot study in which they treated patients with refractory Crohn's disease (CD) with a single fecal microbiota transplantation (FMT) through the mid-gut.<sup>(5)</sup> In the paper, the authors noted that FMT for treatment of intestinal diseases was recorded in traditional Chinese medicine as far back as the fourth century. However, few modern clinical studies exist.

First, the researchers established a new standardized laboratory protocol for FMT. Then, they treated 49 patients, 30 of whom qualified for the study's analysis with at least a 6-month follow-up. Patients underwent a single

FMT, and received a small sustaining dose of Mesalazine. They also received a 'food plan' to follow after FMT. After 1 month, clinical improvement was 86.7% (26/30) and clinical remission was 76.7% (23/30). Patients' body weight also increased.

Evidence indicated that the efficacy of FMT did not depend on the genetic relationship or close contact between the donor and patient, or on the dose of bacteria. The fresh fecal microbiota samples, however, were associated with a higher rate of clinical improvement and clinical remission than frozen microbiota. These findings need to be validated in larger studies.

Authors say that further studies need to test these clinical FMT results against alternative therapies, but that they have shown the potential of their FMT procedure to treat refractory CD.

Dr. Faming Zhang spoke with GMFH about this study.

FMT has been used to successfully treat C. difficile infection. What gave you the idea to use it for patients with Crohn's disease?

C. difficile infection is an acute infection. However, inflammatory bowel diseases or IBDs, including Crohn's disease and ulcerative colitis, are chronic inflammatory diseases. If dysbiosis in IBD is a fact, then we don't know whether dysbiosis is a cause or a consequence of inflammation. We don't know which one comes before the other one, chicken or egg. But it doesn't matter for treatment; this study strongly supports the link between intestinal bacteria and IBD. Our hypothesis is that 'reconstruction' of gut microbiota should be helpful for treating those with Crohn's disease.

In the past 10-20 years, there are more and more cases of Crohn's disease in China. However, 20-30 years ago, Crohn's disease was very, very seldom seen in China.

Why did you study refractory Crohn's disease in particular?

Generally, gastroenterologists have similar options to treat patients with Crohn's disease who have a good clinical response to traditional strategies. However, refractory Crohn's disease is very, very challenging for doctors. So we need to explore new ways for treating refractory Crohn's disease when these patients have no more good choices.

How did you select your FMT donors?

First, they must be healthy, without any infectious disease or other potential diseases. We need to test their various

bacterial inflammatory markers.

I want to highlight another item: it's age of the donors. In our study, our donors were children. In this study, they [ranged] from 8 to 15 years old.

There are two reasons for our consideration of donors' age. The first reason is a safety consideration. Generally for young children they have no sexual life in China, no sexually transmitted diseases. So less risk than adults.

The second reason is a literature evidence consideration. So let's look back into the old, old literature of the traditional Chinese medicine. Doctors suggest using eleven- to twelve-year-old children. Possibly - I just guess - it is this age period that a person has the most wonderful microbiota status in his or her whole life.

Were there any negative effects of the FMT treatment?

From the more than 280 cases [not all of whom were included in this study], no serious adverse events were observed in our center.

Did anything surprise you about the results?

FMT relieved Crohn's disease-related abdominal pain within several hours to one day after FMT. Also, we observed FMT cured some skin lesions, improved lipid profile, and even [improved] sexual function in Crohn's disease.

What are the next steps in your research?

My group is focusing on two things: the first thing is to move standardized FMT forward. The second is to explore why FMT is so powerful against intestinal diseases and other diseases.

We have established a standard clinical flow for FMT, including purification of microbiota in the lab, then transfer to the endoscopy center, and standard preparation of patients before and during the procedure of transplantation. We developed an automatic system (GenFMTer) for isolation of microbiota from stool. I am the principal inventor of this novel system. Now, the operator of the system process in the lab cannot touch the stool, cannot see the stool, cannot smell the bad smell. This is the most important step to move standardized FMT into [the] mainstream.