Gut Microbes May Protect People Having Bone Marrow Transplants

By Julie Grisham, **Sunday, December 2, 2018**

Jonathan Peled speaks during a press conference at the 2018 meeting of the American Society of Hematology. Photo credit: ASH/Scott Morgan

Summary

> For the first time, researchers have found that having a healthy balance of microorganisms in the body before a bone marrow transplant is associated with higher survival rates after the transplant.

Update: On February 27, 2020, Dr. Peled, Dr. van den Brink, and their collaborators reported updates from this research in the ***New England Journal of Medicine***. The expanded analysis now includes 8,767 stool samples from 1,362 people who have had allogeneic stem cell or bone marrow transplants at four centers around the world.

The findings confirmed that a having a greater diversity of species in the intestinal microbiota is associated with a lower risk of death after having a transplant. They also report for the first time that having a lower diversity of microbiota before transplant resulted in a higher incidence of graft-versus-host disease. The patterns were the same across all geographical regions included in the study.

Original post: One of the most serious complications of **blood stem cell or bone marrow transplants (BMTs)**, which are used to treat many types of blood cancer, is graft-versus-host disease (GVHD). In this condition, a donor's immune cells attack the vital organs of a transplant recipient. It can cause death in some cases.

In the past few years, researchers from Memorial Sloan Kettering and other institutions have found that a transplant recipient's microbiota plays an important role in their survival after a BMT. (The microbiota is the community of organisms, or flora, that live in the body, especially in the gut.) Now, for the first time, investigators have found an association between the health of the microbiota before a transplant and a person's survival afterward. The findings were presented December 2, 2018, at the annual meeting of the American Society of Hematology (ASH).

"Patients who went into the BMT process with a gut flora that was already disrupted had a higher risk of death after the transplant," says the study's senior author, **Marcel van den Brink,** Head of MSK's **Division of Hematologic Malignancies**. "The thing that we keep coming back to is that preserving the commensal flora in the microbiome is good for transplant patients." Commensal flora are microbes that live in the body without causing disease. In some people, they may be beneficial.

The Forgotten Organ

Many of those who study the gut microbiota refer to it as the "forgotten organ." It can have a huge impact on someone's health. But scientists are still learning what makes it healthy or damaged, and what can be done to correct that damage.

"There are as many bacterial cells as there are human cells in our bodies," says first author **Jonathan Peled**, an MSK medical oncologist who specializes in BMTs. "In addition, these bacteria are really important for the way our bodies function."

"Before someone has a BMT to treat their cancer, we do a lot of screening tests to make sure they are otherwise healthy. We look at things like their heart, lung, and kidney function," says Dr. van den Brink, who runs a lab in the **Sloan Kettering Institute's Immunology Program**. "This study suggests that we should also screen the microbiota. If we find out that it's in bad shape, we could do something to repair it."

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Jonathan Peled
medical oncologist

Dr. Peled adds, "This study opens the door to repairing the microbiota in the pretransplant period. Because this is a time when we're usually not in a rush to move forward with treatment, it's also a good time to look for ways to do this before continuing the transplant." Interventions that could improve the health of the microbiota include changes to diet, using or avoiding certain antibiotics, and fecal transplants of healthy gut microbes.

MSK doctors are already conducting research on fecal transplants that make use of a patient's own stool. The stool is preserved before the BMT and given back to the patient after the process. **A recent study** led by MSK physician-scientists Eric Pamer and **Ying Taur** found that fecal transplants are effective in restoring the balance of healthy microbes that is lost during a BMT. Researchers also plan to study the safety of providing fecal transplants with material from a healthy donor. Donor stool may ultimately prove to be a better option for people who come to a BMT with a microbiota that's damaged.

Throwing Off the Healthy Balance of the Gut

In the analysis presented at ASH, the researchers studied 1,922 stool samples from 991 people having allogeneic BMTs. “Allogeneic” means the blood or marrow stem cells come from a donor. (In the other type of transplant, an autologous procedure, a patient’s own blood cells are stored before treatment and later infused back into the body.) The people were treated at MSK and three other hospitals. The samples were evaluated for a range of bacteria types, including commensal strains and those that are known to cause disease.

The investigators found that, on average, the people about to have BMTs had decreased diversity of bacteria in their guts. They also found that different strains were dominant, compared with healthy volunteers. This was a new finding, but it was not surprising. Most people with blood cancer who need transplants have gone through months or years of treatment with chemotherapy drugs and antibiotics that throw off the normal, healthy balance.

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Diversity in the microbiota is important because commensal bacteria help keep more dangerous strains in check. Previous studies have also shown that certain commensal strains actually provide specific benefits for people having transplants. Some strains release substances that protect the walls of the intestines, for example.

In the current study, only 10 to 30% of patients had what researchers considered a balanced gut flora before their transplant. The more the ecology of the microbiota was disrupted, the more likely it was that patients had fatal complications from GVHD. However, the researchers emphasize that this study showed only an association, not direct causation.

A Study with a Broad Geographic Scope

Investigators at three other transplant centers also participated in the research and contributed patient samples: Duke University School of Medicine in Durham, North Carolina; Hokkaido University in Sapporo, Japan; and University Hospital Regensburg in Germany. Different locations were included because other research has shown that microbiotas across geographic regions vary widely. Factors like environment and diet are thought to play a role.

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physician-scientist

All of the samples were analyzed in MSK labs, Dr. Peled says, improving the validity of the results across the sites.

“One of the main findings of this study was that the injury patterns that we saw in people’s microbiotas were comparable across geography,” he concludes. “This suggests that if we find interventions to correct these imbalances at one center, they will also apply to people being treated in other parts of the world.”

Dr. Peled received research funding from Seres Therapeutics.

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