insights
INNOVATIONS IN TREATMENT
National Hemophilia Foundation

National Hemophilia Foundation
for all bleeding disorders

FREQUENTLY ASKED QUESTIONS ON GENE THERAPY

GENE THERAPY DEFINED:

What is gene therapy?
Gene therapy is a treatment where new working genes are introduced into a person's cells to fight disease. In the case of hemophilia, the new genes give the body instructions on how to make factor. There are different kinds of gene therapy, including gene transfer, gene editing, and cell therapy.

How does gene therapy work in hemophilia?
A working gene has clear directions that tells the cell how to make factor. In gene therapy, a working gene is carried into the liver cells of a person with hemophilia. Once the working gene reaches the cells, they should begin producing factor.

What is a vector?
At this time, gene therapy focused on treating hemophilia uses viral vectors. A vector is a virus that has been changed to remove the illness causing (viral) material. It is used as a carrier to bring the new, working genes into a person's cells. Viral vectors are used in gene therapy because they are very effective at getting into cells.

What vectors are being used in gene therapy for hemophilia?
The most commonly used vectors in hemophilia are called adeno-associated viruses, or AAV. These vectors do not carry any infectious material, meaning they do not cause viral infections. They are used to deliver working genes into liver cells in the body so that they can start producing clotting factor.

What are the differences between gene editing, gene transfer and cell therapy?
Gene transfer puts genetic information into a vector, which then carries the working copy of a gene to a person's cells. Once inside the cell, the new, working gene allows the cell to start making factor. Gene editing tries to "fix" the part of a gene that isn't working. By editing the genetic directions, the cell can then start to make factor. Cell therapy transfers cells that work well into a person to treat disease. These cells are created to produce clotting factors. They are contained in specific materials that prevent them from attack by the patient's immune system. These cells are implanted inside the body and will help the individual make their own factor.

What is CRISPR?
CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats. CRISPR is a way to edit a non-working gene. Instead of bringing new copies of the working gene using a vector, as in gene transfer, CRISPR actually tries to fix the patient's non-working gene within the cell. One way to think about the difference between gene transfer and CRISPR is to pretend you have a table with two broken legs. With gene transfer, someone would bring a new, unbroken table. The old table would remain without being of any use. With CRISPR, someone would fix the two broken legs still attached to the table. The table would be still be the original table but now improved and working. While CRISPR is exciting science, federal laws currently prevent the use of CRISPR in humans.

ELIGIBILITY:

Who can undergo gene therapy?
At this time, gene therapy for hemophilia A and B is being studied in clinical trials to determine how well it works and how safe it is. This means only people who are part of a research study can receive it. In general, individuals able to participate in this type of study are:

- Male
- 18 and older
- Have severe hemophilia A or B (factor levels of less than 1%) without inhibitors
- Have no evidence of hepatitis and if they have HIV, it must be under good control
- Have no evidence of liver dysfunction (such as abnormal liver enzymes or abnormal liver biopsy)
- Have no detectable neutralizing antibodies against the vector. Antibodies are created by the body to protect us against potentially harmful things such as viruses and germs. Once our bodies make antibodies against something they neutralize or destroy that target as soon as it gets in contact with them.
- Otherwise healthy (no diabetes, history of cancer, heart disease, glaucoma, high blood pressure, etc.)

Your healthcare provider can help you decide if participating in a study to receive gene therapy is right for you.

Can my child undergo gene therapy?

At this time, gene therapy for hemophilia is not available for people under 18 years of age. Gene therapy for hemophilia targets the liver cells. Children's livers continue to grow until, at least, age 12. As the liver grows, the effects of gene therapy is reduced. As we learn more about gene therapy safety, there may be opportunities for enrollment of children.

Can women with hemophilia receive gene therapy?

At this time, gene therapy is not being studied in women with hemophilia.

WHAT CAN I EXPECT:

Is gene therapy a cure for hemophilia?

Current studies have shown that patients with hemophilia who undergo gene therapy may see their factor levels increase – sometimes to normal levels. They may also be able to avoid some factor infusions for a long period of time. However, studies are still ongoing to determine how long these benefits will last. As with many other treatments and medications, each patient that receives gene therapy may have different results, meaning some patients may reach higher factor levels than others.

Are there gene therapy treatments for both hemophilia A and hemophilia B?

Yes, currently there are several different clinical trials for both types of hemophilia.

What can I expect my factor level to be once I undergo gene therapy?

This depends on many things. Response to gene therapy varies from person to person and can decrease over time. So far, clinical trials have shown an increase in factor levels after gene therapy. However, we still don't know if it will work on everyone, how high the resulting factor levels will be, and how long these higher levels will last.

Will my factor levels change in the future if I undergo gene therapy?

Current clinical trials data have shown a reduction in factor levels over time. This means that factor levels may increase soon after you receive gene therapy but decrease over time.

When will gene therapy for hemophilia be available to everyone without enrolling in a clinical trial?

Currently, several ongoing clinical trials for both hemophilia A and B are showing promising results. Clinical trials are done to ensure that gene therapy, or any other treatment is safe and effective. Gene therapies are currently in phase 2 and 3. NHF will continue to closely monitor the progress of these trials.

How long can I expect the effects of gene therapy to last?

At this time, no one really knows the answer to this question. There are several clinical trials underway that have shown increased factor levels lasting more than seven years.

Will I still need factor if I receive gene therapy? What if I have an accident, injury or need surgery?

The need for factor after undergoing gene therapy will depend on how much factor your body makes and how long it lasts. Each person's response to gene therapy will likely be different and will require an approach that is specific to them. This is a topic you should discuss with your provider.

If I undergo gene therapy and it stops working, can I try again in the future?

Not currently. At present, gene therapy for hemophilia can only be done once. It is possible that this could change in the future.

Once I undergo gene therapy will I still need annual checkups at my HTC?

Yes. It is very important that you continue seeing your healthcare team after undergoing gene therapy. They will need to monitor the effects of this new therapy long term to make sure that it works as expected and to monitor any problems that may arise.

Can I stop or turn off gene therapy?

No. Once you undergo gene therapy the changes made to your cells cannot be undone. It cannot be reversed or stopped.

RISKS ASSOCIATED WITH GENE THERAPY:

What are the risks associated with gene therapy?

Some possible risks associated with gene therapy include a strong immune system reaction, that it goes to another cell instead of the liver cell, that it causes liver damage, that it gets inserted into the genes of the cells and exposing others to the vector. There are also many unknown risks that we do not understand at this time.

What is vector shedding?
It is the process by which the viral vector leaves the body once it is no longer needed. The virus is released through urine, feces, blood, saliva and semen.

What happens if I undergo gene therapy and my factor levels get really high?
In some cases, gene therapy has led to factor levels above the normal range. If this happens, you will need to be closely monitored by your hemophilia treatment center. Although high factor levels may be linked to the development of dangerous clots, this side effect has not been reported in clinical trials.

GENE THERAPY AND REPRODUCTION:

Can I pass the effects of gene therapy to my children?
No. Gene therapy to treat hemophilia corrects the non-working gene only in the person who receives it. The viral vector carries a working copy of the factor VIII (8) or factor IX (9) gene to the liver cells, providing them with the instructions of how to produce the missing factor. Gene therapy does not correct genes passed on to children.

Should patients who undergo gene therapy bank sperm?
After undergoing gene therapy, the body can take up to several months to get rid of the vector used. This process is called viral shedding. The vector leaves the body through different bodily fluids such as semen, blood, urine, feces and saliva. Although the risk for the vector to affect sperm is low, men who undergo gene therapy are asked to use a barrier contraceptive method such as condoms to prevent pregnancies for an extended period of time after receiving gene therapy. If you are considering having a child soon after receiving gene therapy, you should discuss banking sperm with your doctor before doing so.

Will gene therapy affect my ability to have children?
No, gene therapy will not affect your ability to have children. However, because the vector is present in semen for a long period of time after receiving gene therapy, it is recommended that men use a barrier contraceptive method, such as condoms, to prevent pregnancies until the vector is no longer there.

GENE THERAPY CLINICAL TRIALS:

Can I get gene therapy today outside a clinical trial?
Not right now. There are no gene therapy treatments for hemophilia A or B that have been approved by the FDA. At this time, your doctor cannot prescribe gene therapy treatments until the FDA determines they are safe and effective.

How can I find out about on-going gene therapy clinical trials for hemophilia?
You can find information on clinical trials at www.ClinicalTrials.gov. Enter “hemophilia” in the text box labeled “condition or disease” and “gene therapy” in the one labeled other “terms”. If you want to only find trials available in the United States, then select that option in the text box labeled “Country”. And then select the blue button that says Search. Once you get presented with the options you can use the filters on the left to select trials based on recruitment status, age, and sex. In addition, your HTC provider can also direct you to current clinical trials and answer specific questions you may have.

GENE THERAPY AND INHIBITORS:

Will gene therapy cause me to develop an inhibitor to my factor?
Probably not, but this is not yet known. Although current gene therapy trials have not studied persons with a higher risk of getting an inhibitor, they have not shown a higher risk for those who have.

Can I receive gene therapy if I have an inhibitor?
No. At this time, clinical trials are not enrolling individuals with an active inhibitor or those who might still be at risk to develop one. That is, those who have had less than 150 exposure days to factor replacement therapy.

PSYCHOSOCIAL ISSUES AND GENE THERAPY:

What are the psychosocial issues that I should expect if I undergo gene therapy?
You may have conflicting feelings after you undergo gene therapy or any other major life change. Examples could include guilt, feeling of not belonging to the community or fear of how the therapy might impact you in the future. This is completely normal. It is important that you speak with your HTC or primary care provider who can help you understand these feelings. Your HTC may also be able to put you in touch with another patient who is also enrolled in a gene therapy trial.

Will I still be part of the bleeding disorders community?

The bleeding disorders community is warm and welcoming, regardless of a change in your health status. You will always be a member of the community. You have much to offer, and your experience and knowledge can be very beneficial to others.

Will I still have hemophilia if I have normal factor levels after undergoing gene therapy?

Yes. Because gene therapy is relatively new, we don't know how high your factor levels will be and how long will they last. Factor levels may end up in the mild, moderate, or normal range and, even so, may change over time. While you may rarely need infusions of factor, you may still need it for surgeries, procedures, or after an accident. For that reason, you will need to stay in touch with your hemophilia treatment center and your community.

Will I still be able to go to the HTC?

Yes, please do! It is very important to be monitored for changes in overall physical health, including laboratory tests, as well as emotional health. Also, any issues you had prior to gene therapy (ex. joint issues) will need to be monitored as well. Your hemophilia treatment center will always be an important partner before and after gene therapy.

GENERAL INFORMATION:

How is gene therapy given?

Gene therapy is a one-time intravenous (IV) infusion done in a medical facility by doctors and nurses. Patients receiving their infusion are always under close supervision. The infusion can last anywhere from minutes to a few hours.

Where will I receive gene therapy?

At this time, gene therapy is only available to people who are enrolled in a clinical trial. Infusions only occur in hemophilia treatment centers participating in clinical trials.

Will my insurance company pay for gene therapy?

NHF supports access to all FDA approved treatments and therapies, and has been engaged from early on with payers, developers and other interested organizations, to be a voice for consumers who wish to receive these novel therapies may do so. NHF strives to assure payers recognize these treatments should be delivered by expert providers found within HTC's, the only recognized center of excellence model purposely established to care for patients with bleeding and clotting disorders.

Social Media:

Stay connected to the latest gene therapy news on social media by following NHF on social media:

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