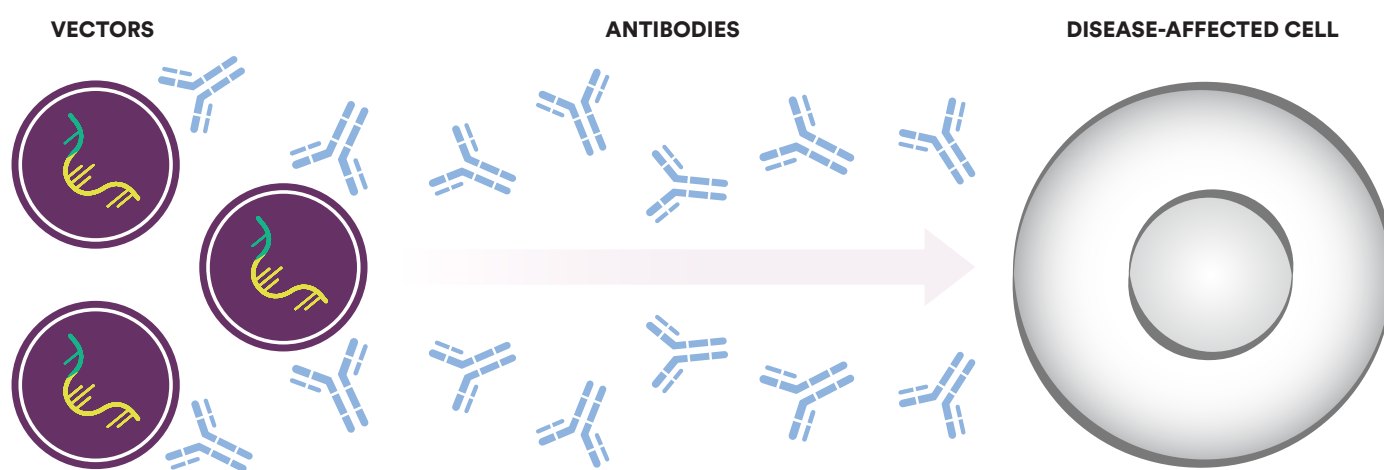


This fact sheet will provide valuable information on **antibody testing**, which is one important factor in determining eligibility for gene therapies currently being studied in clinical trials.¹ In a clinical trial, other eligibility factors may include age, type of genetic mutation, baseline mobility and function, and prior exposure to an investigational or commercially available therapy.²

Why does antibody testing play a role in determining eligibility for a gene therapy?

Prior to treatment, individuals must be tested for **preexisting antibodies*** because they may prevent the therapy from working as intended.^{1,3}

Gene therapies are delivered via a **vector**, which aims to deliver functioning genes to disease-affected cells in the body.⁴ The vector is a delivery vehicle that aims to bring the functioning gene into target cells.⁵ The vector is selected based on its ability to get into these target cells. One of the most common vectors used in gene therapy is the adeno-associated virus (AAV) vector. Because vectors are not naturally found in the body, the immune system may respond to them as if they are foreign invaders and work to eliminate them with the help of antibodies.^{4,6} For this reason, antibody testing plays an important role in determining eligibility for therapy.^{1,3}



How do preexisting antibodies develop against gene therapy vectors?

Individuals may develop preexisting antibodies that recognize a gene therapy vector **even if they've never received a gene therapy before**. Some viruses naturally present in the environment are similar to vectors used in gene therapy, and if exposed, an individual's immune system can make antibodies against the virus that also recognize the vector.⁶ Currently, there is no way to prevent the development of these naturally occurring antibodies or to know if an individual has been exposed to one of these viruses without an antibody test.⁷

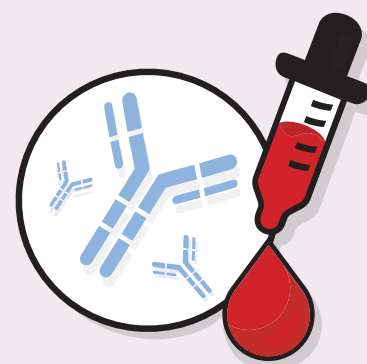
Importantly, approved Duchenne therapies like steroids and exon skipping **do not create antibodies**.^{8,9}

How are antibody tests used to help determine eligibility for a gene therapy?

Antibody testing is the **only way** to determine if an individual has preexisting antibodies that may prevent a gene therapy from working as intended.^{1,6}

Helpful definitions

- **Antibody titer:** a measurement of the amount of antibodies in a blood sample that can recognize a vector¹⁰
- **Seropositive (elevated):** preexisting antibodies are detected in the body at levels **above** a predefined threshold. Individuals who are seropositive are **ineligible** for gene therapy or clinical trials.¹
- **Seronegative (not elevated):** no preexisting antibodies are detected in the body, or they are present at levels **below** a predefined threshold³

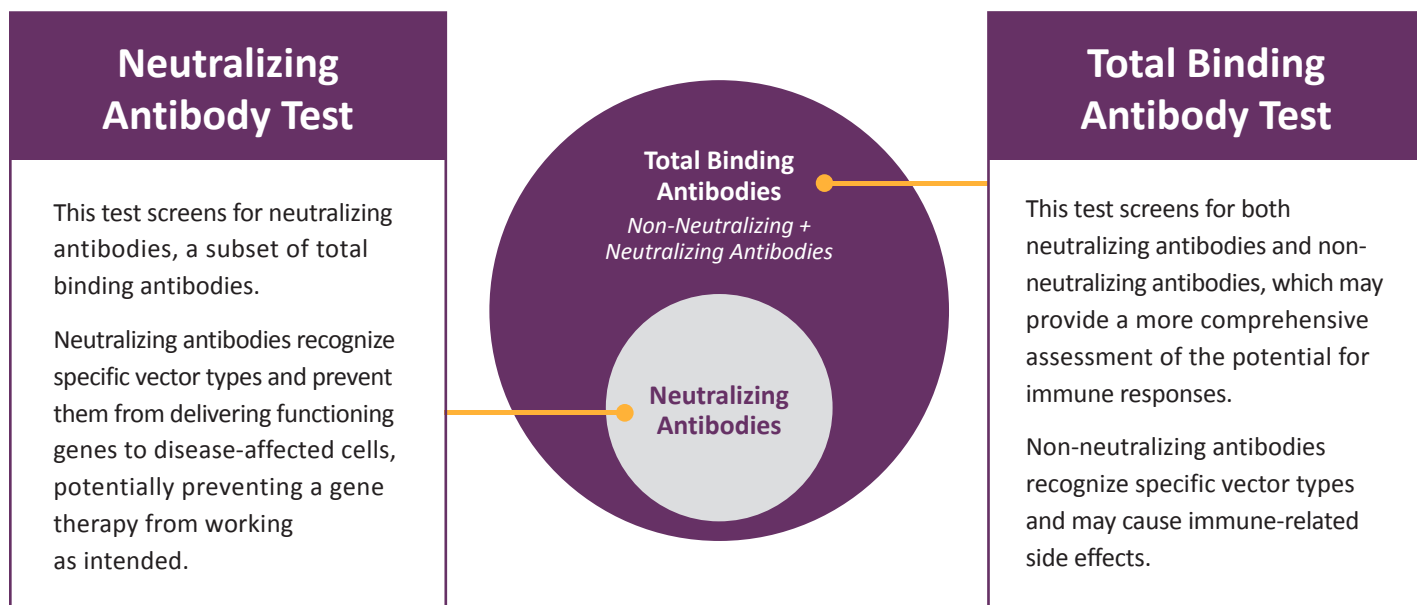


Individuals will need to take the antibody test **specific to the gene therapy they are considering**. The type of antibody test needed may differ depending on the vector used and the therapy's manufacturer. Currently, **no universal antibody test exists**.¹¹

Additionally, the concentration of antibodies in the body can change over time, and an individual who was initially seronegative can become seropositive. That's why antibody testing **must be performed at the time** that an individual is being considered for participation in a gene therapy clinical trial, regardless of whether they have received an antibody test before.^{1,3}

*Preexisting antibodies are those already present in the body that may recognize a gene therapy's vector.⁶

Two different types of antibody tests may be used in clinical trials¹²:



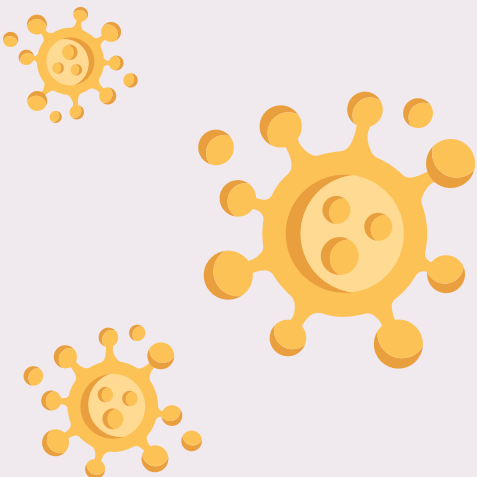
When considering a clinical trial for gene therapy, ask your doctor what type of antibody test will be used.

What options are available to those who are ineligible for a gene therapy?

Unfortunately, once someone has been shown to have preexisting antibodies above the eligibility threshold, they will not be eligible for a clinical trial involving that specific gene therapy or available approved gene therapies. Moreover, if an individual has a high antibody titer for one vector, it is unknown what that will mean for antibody testing results for other vectors. Individuals must be tested for eligibility for each gene therapy being considered, even if the vector is the same. The science and our understanding of overcoming preexisting antibodies to gene therapies is evolving. Speak with your doctor about gene therapy clinical trials or available, approved therapies.^{3,6}

Researchers are in the early stages of exploring different strategies to expand eligibility for gene therapies. Approaches under investigation include treatments that break down or filter out (plasmapheresis) preexisting antibodies in the blood, designing vectors that can evade recognition by antibodies, and finding new delivery vehicles for the therapy that are not recognized by antibodies at all.^{4,7}

For more information, please visit [Duchenne.com](https://www.duchenne.com)



Can a COVID-19 or flu vaccine cause preexisting antibodies against a gene therapy?

To date, there is no evidence to suggest that current mRNA (Pfizer and Moderna) and adenovirus-based (Johnson & Johnson) COVID-19 vaccines or flu vaccines can cause the production of antibodies that interfere with these vectors.¹³ Only **adeno-associated virus (AAV) vector-based** vaccines or therapeutics have the potential to promote production of antibodies against the gene therapy vectors currently being studied for neuromuscular diseases. There are currently no AAV-based COVID-19 or flu vaccines approved.¹³

Adeno-associated viruses are not the same as adenoviruses!

Although **adeno-associated virus (AAV)** and **adenovirus** have similar names and are both being investigated in gene therapies, they are very different viruses. Antibodies that recognize adenovirus vectors are not expected to be the same as antibodies that recognize AAV vectors.¹⁴⁻¹⁶

For more information on COVID-19 vaccines and eligibility for gene therapy clinical trials, please see our community bulletin on [Sarepta.com](https://www.sarepta.com).

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