Autism Spectrum Disorder (ASD) includes several conditions that were previously considered separately. These include Autism, Asperger’s Syndrome, Childhood Disintegrative Disorder, and an unspecified form of Pervasive Developmental Disorder. Patients with ASD show a wide range of variations in symptoms, condition severity, and functional disability (Geschwind, 2009). Although scientists have not yet been able to determine the exact cause leading to ASD, it has been theorized that the disturbances caused during the embryonic stages may be responsible (Courchesne et al., 2019).

ASD may be divided into two main symptom categories: The first one is reduced social interaction and the second one is repetitive behaviors, curiosities, and aggressive actions. ASD can sometimes be detected at eighteen months or younger. The recent figures estimate ASD global prevalence to be approximately one in 100 children (World Health Organization).

Existing Treatments

Traditional treatments for autism patients include speech therapies, social interaction training, applied behavioral analysis and use of psychotropic drugs (Thibaut, 2017). While early behavioral interventions often improve functioning and outcome, there are currently NO medications specifically approved for the core symptoms of ASD. They are usually prescribed “off label” for the associated symptoms of irritability or hyperactivity.

Alternative therapies include hyperbaric oxygen management (Oberman, Rotenberg, & Pascual-Leone, 2015) music therapy, cognitive behavioral
therapy, and fast learning therapies (S. R. Sharma, Gonda, & Tarazi, 2018).

The use of complementary and alternative medicine (CAM) is common in kids with ASD, despite the lack of research and potential side effects. Some regularly used CAM therapies, such as methyl B12, oxytocin, ginkgo biloba, secretin, and chelation therapy, have been found to be ineffective. Hence, it is imperative that safer alternative therapies such as stem cell therapy be investigated and promulgated further (Shuai et al., 2020).

The key point here is that to date, the conventional and alternative therapies that exist are typically just not satisfactory to parents. R3 receives many calls a day from parents around the world who have tried traditional therapies with unsatisfactory results.

Let’s discuss stem cell therapy for ASD and the risk/benefits associated. First of all, researchers have not been able to pinpoint an exact cause for ASD. There are quite a few theories, but nothing has been universally agreed upon. Secondly, no cure for ASD currently exists. So the focus has been on mitigation.

**Autologous Stem Cell Procedures**

Autologous stem cell procedures involve harvesting tissue from the patient to use, which is either bone marrow or adipose. That tissue is then processed either immediately or over a period of weeks to administer back to the patient.

In a review of published clinical trials looking at stem cell therapies for ASD, R3 Stem Cell noted that Sharma et al performed several studies utilizing bone marrow mononuclear cells for ASD (Shamim et al, 2023, Regenerative Medicine). The cells were delivered intrathecally (into the spinal cord), with no significant adverse events being seen (temporary nausea/vomiting were reported).
After six months of follow up, there was improved concentration, stable sleep patterns, proper eye contact, great social interaction and improved memory were recorded. There have not been published clinical trials on adipose stem cells for ASD to date.

There have been a few well documented clinical trials evaluating autologous umbilical cord blood treatment for ASD. In 2018 a phase I/II clinical trial was conducted using autologous umbilical cord blood (UCB) in patients with ASD by Sutter Pediatric Neurology (Sacramento, CA, USA). A total of 30 patients were enrolled for the randomized, triple-blinded (participant, care provider and investigator), placebo-controlled and crossover study. An age range of 2–7 years was maintained. The subjects were infused with autologous UCB and placebo (saline). The dosage used was a minimum of 10 million total nucleated cells/kg in one infusion of 60 ml of study product. Twenty-nine patients completed the post-treatment follow-up.

The outcome measures used included CGI, expressive and receptive one-word picture vocabulary tests, Stanford–Binet Fluid Reasoning and Knowledge and Vineland Adaptive Behavior and Socialization. According to the study, none of the participants experienced serious adverse events, nor did they have to be hospitalized as a consequence of cellular therapy during the period of the study [44]. The researchers noted positive results, especially in the outcome measures for social activities; however, when statistically analyzed, no significant changes were obtained in the outcomes. Nevertheless, it may be inferred from the study results that autologous UCB infusions may be safely used in ASD subjects.

A safety study with 25 autistic children between the ages of 2 and 6 years for phase I clinical trials was conducted by Duke University. The participants selected had their
own autologous UCB unit, and no masking was done. The researchers discussed the therapeutic utility of UCB by-products for the treatment of children with ASD. In this study, the intravenous mode of delivery for treatment was chosen. A dose of $1\text{–}5 \times 10^7$ cells/kg was given to the participants.

After the evaluation of the adverse and serious adverse events for a whole year, the researchers found this treatment to be safe for usage for ASD patients. The results indicated a general improvement in the symptoms specific to autistic children. These also included speech and verbal/nonverbal socialization skills.

A phase II study was completed in 2019 by researchers at Duke University, using single intravenous autologous or allogeneic, unrelated UCB on 180 participants. A minimum banked total nucleated cell dose of $\geq 2.5 \times 10^7$ cells/kg or $\geq 4/6$ HLA-matched allogenic, unrelated UCB was used. Once again, the researchers noted UCB to be safe for administration, either autologous or allogenic. Significant improvement was observed in the communication activities involving toys and employing focus. The researchers observed insufficiency of the single dose of UCB toward alleviating symptoms of autism or improving social skills.
Donor Stem Cell Procedures

The 2019 study mentioned in the previous paragraph included both autologous and allogeneic umbilical cord tissue, so it spans into this section.

Researchers from Shandong Jiaotong Hospital Jinan, Shandong (China) conducted a phase I/II clinical trial to measure the safety, feasibility and efficacy of UCMSCs and CBMNCs in autistic children. It was an open-label and parallel intervention in which 37 autistic subjects were enrolled. Patients received both cord blood cells and umbilical cord mesenchymal stem cells. At the time of cell therapy, no adverse event was measured except for low grade fever.

The significant changes observed included improved social and behavioral withdrawals, enhanced eye contact, less emotional and aggressive response, adaptability, and less hyperactivation and unstable speech patterns. At 24-week follow-up, the results were compared with the control group, and considerably higher improvements were seen in the combination group.

A very well done study by Riordan et al (2019, Stem Cells Transl Med) included 20 participants receiving a total of 144 million umbilical cord mesenchymal stem cells over 4 treatments. While the study has been retracted (due to patients paying for treatment), adverse events included fatigue, headache, fever, hyperactivity, anxiety and swelling. All of these were temporary.

Periodic psychiatric evaluations showed that the group of children who presented improvements in efficacy variables also manifested increased awareness, and noticeable improvements in social communication (both verbal and expressive) and motor ability, despite causing an increase in anxiety and emotional liability in some of them. According to the researchers, “From our previous clinical observations, the therapeutic effect of MSC infusions often declines between 3 and 6 months after administration, likely due to the immune evasive properties of MSCs that allow them to persist in the body before being eliminated.”

Stem Cell Derived Exosomes

R3 Stem Cell’s Centers of Excellence globally include umbilical cord stem cell derived exosomes with umbilical cord stem cells to provide enhanced results. Exosomes are lipid bound vesicles (acellular) produced by cells which contain a plethora of growth factors,
cytokines, mRNA and other proteins.

They are exceptionally helpful in cell to cell communication, and very effective for reducing inflammation when they become ingested by their recipient cell. They act as shuttles to send nucleic acids and proteins to other cells, in this way, allowing cell-to-cell communication and transporting molecules among both close and distant cells. In general, these released proteins are important regulators of intracellular information.

Exosomes could be the mediators of many stem cell-associated therapeutic activities. Considering they are 100 times smaller than stem cells, they do not have any issues crossing the blood brain barrier to reach the central nervous system from the bloodstream. (Alessio et al, Int Jour Env Res Pub Health, 2020).

R3 Stem Cell’s Experience

R3 Stem Cell has over 45 Centers of Excellence globally with a presence in six countries. Autism is one of the top conditions for which therapy with stem cells and exosomes is performed. There are several factors R3 has taken into consideration when optimizing these therapies for children.

First of all, safety with these treatments is paramount. In line with ALL of the studies mentioned in this guide, R3 Stem Cell has not seen significant adverse events. Temporary issues such as low grade fever, nausea, headaches, dizziness are frequently seen.

The biologics utilized undergo rigorous screening processes for all types of contaminants and communicable diseases. Only if all the testing is negative, are the biologics able to be used.

Results

Secondly, effectiveness is critical. One of the main reasons R3’s Centers have become so popular for autism therapy is the success rates. Over 85% of families are exceptionally happy with their child's results. The results seen span the categories of behavior and communication. Whether it’s verbal or non-verbal improvements, the results are typically obvious.

A lot of children with ASD are hyperactive and/or aggressive with their family or friends. In line with the results Duke University saw, R3’s patients typically see a significant reduction in these behaviors.

Affordable

And third, affordability is key. Because stem cell therapy for Autism is not a

Guide to Stem Cell Therapy for Autism

R3StemCell.com or Call +1 (844) GET-STEM
cure, it’s important to make it affordable. Repeat therapies can help gain additional improvements for ASD children. So a lot of families seek additional treatments at R3 Stem Cell every six to eighteen months. It’s not mandatory, but something we see a lot.

Unfortunately, stem cell clinics in Colombia, China and Panama charge over $20,000 USD for autism treatment. Because the one treatment cost so much, how are families supposed to budget for that every year?? R3 Stem Cell’s fees are less than half that for 100 million high quality stem cells!

Protocol
When it comes to stem cell and exosome therapy for autism, R3’s protocol is safe and effective. The anesthesiologists at R3’s Centers are experts in the intrathecal application. It’s basically a “reverse” spinal tap procedure and allows millions of stem cells to safely be administered into the central nervous system.

Conscious sedation may be administered, which allows the child to be awake but not aware of the procedure. It is not general anesthesia, it’s simply a fast acting medication like Versed.

R3 Stem Cell administers a multivitamin infusion along with the stem cells,
which helps to activate the cells for best results. The umbilical cord stem cells are administered IV as well as intrathecal.

R3’s experienced providers use clinical judgment and best practice protocols to decide on the amount of stem cells necessary for best results. This may include from 3 to 6 million stem cells per kilogram, and from 30 billion to 180 billion exosomes as well.

Treatments may occur on one day, or be separated into two days for patient safety. A family member is typically allowed in the room. R3’s procedure rooms have intensive monitoring equipment.

Bottom Line
There are plenty of naysayers who say the following:

1. It’s not safe: There are no well performed studies showing significant adverse events to date, and R3 hasn’t seen any either.

2. Effectiveness isn’t proven: In R3’s experience, the results are excellent and noticeable by the family 85% of the time. Numerous studies, some of which are reported in this Guide, show the clinical effectiveness.

3. More research is needed: R3 hears this frequently from providers who are offering only conventional therapies. The families who have their child being treated with those providers are not satisfied with the results. At what point does stem cell therapy become “acceptable” to these laggard providers??

R3’s Experience
For the past decade, R3 Stem Cell’s Centers globally have performed over 23,000 regenerative procedures in six countries. Hundreds have been for ASD. Patient satisfaction across all conditions treated is 85%!

R3 combines safety, effectiveness and affordability for the autism therapies. Internationally, the Intellicell is used, which is culturing the most active mesenchymal stem cells to create the “smartest” stem cell in the world!

R3 Stem Cell offers free consultations for families to discuss whether regenerative therapy is indicated for their children. Simply call +1 (844) GET-STEM or +1 (480) 808-7057 to schedule yours!