

Human Stem Cell Therapy at the Institute of Regenerative Medicine A White Paper

Introduction

Scientists from around the world are extremely excited about the ability of human stem cells, as progenitor “master cells,” to differentiate into any of a variety of the body’s tissues and, therefore, potentially treat a wide range of diseases and disorders. This enthusiasm is manifested by the enormous, varied and expanding research on stem cells. For example, a Medline search of articles in medical journals identifies more than 8400 with “stem cells” in the title since 1964 (including more than 900 clinical trials), with the number of publications increasing four- to eight-fold each decade. The topics of stem cell research and potential therapies transcend science and medicine, and have crossed over to political, social and religious domains.

Despite this enormous and growing body of research, relatively little has been published in the western literature on actual clinical applications, other than of adult stem cells, which may have limitations (discussed below). Very little has been published on clinical applications of the other two major sources of stem cells, fetal and embryonic stem cells, owing to negative political and religious environments. Yet, as described below, fetal stem cells may have therapeutic advantages over embryonic and adult stem cells. Moreover, despite the relative dearth of publications on fetal stem cell applications in western literature, medical professionals in Russia and the Ukraine have been recording and reporting clinical experience with these cells for more than 20 years.

The Institute of Regenerative Medicine (IRM) has established a clinic in Barbados, with the permission of the government, to begin providing stem cell therapy to patients. IRM will primarily administer fetal stem cells (i.e., from elective abortions), but is also beginning to investigate adult autologous and allogenic stem cells (e.g., from cord blood). IRM fetal stem cells are from the Institute of Cryobiology and Cryomedicine (and affiliated institutes) in the Ukraine, which processes and prepares the cells according to patented procedures. This white paper summarizes some of the data on clinical experiences with the type of fetal stem cell therapy used by IRM (it does not attempt to review evidence related to clinical applications of other types and sources of stem cells).

Stem Cell Sources

It is becoming increasingly recognized that not all stem cells are created equal. For example, **embryonic stem cells** are derived from a blastocyst, the hollow sphere of cells that develops approximately 5-6 days after an egg is fertilized. (Note: between the seventh and ninth day, the blastocyst attaches to the uterus, and begins to develop and grow. From this point until about eight weeks it is generally referred to as an “embryo”; from eight weeks on it is referred to as a “fetus.”) Because these blastocyst cells can differentiate to become any of the more than 200 types of cells in the body, they are referred to as “pluripotent.” However, too much “versatility” may be harmful, as some studies suggest human embryonic stem cells may form tumors call teratomas.¹

Fetal stem cells are typically derived from electively aborted fetuses of 5 to 12 weeks gestation. At this stage, the stem cells are more tissue-specific (e.g., fetal stem cells in the liver tend to generate liver and blood cell families); thus these stem cells are generally designated as

“multipotent.” However, some research suggests that at least some multipotent stem cells may be more versatile than first thought and may, under the right circumstances, become pluripotent.² Nevertheless, fetal cells may have an advantage over embryonic stem cells in that, being less versatile, they may not form teratomas.

Additionally, up until week 12, fetal stem cells (as well as the embryonic stem cells which preceded them) have a very important property: they have little to none of a certain protein on their surface (Class II HLA) which otherwise can trigger a rejection reaction. Thus, tissue matching – used in blood transfusions, organ transplants, and allogenic adult stem cell transplantation – is not necessary when transplanting embryonic or fetal stem cells.

In the U.S., scientists have proposed methods for preparing and cryopreserving stem cells from fetal tissue for later clinical use. Additionally, to avoid any incentives for abortions, procedures have been recommended that separate the abortion decision from the donation decision, and preserve confidentiality between donor and recipient.^{3,4,5} Similar recommendations have been made in the Ukraine.^{6,7}

Currently, the chief sources of **adult stem cells** are bone marrow, the bloodstream, fat tissue and cord blood. The stem cells derived are blood (hematopoietic) precursor cells, i.e., they generate the major blood cell types: red blood cells, white blood cells and platelets. Thus, these adult stem cells are also multipotent, though less versatile than multipotent fetal stem cells. Some research suggests that blood stem cells may, under the right circumstances, become “pluripotent” and able to generate other cell families.⁸ Other types of multipotent stem cells exist in different tissues, but scientists have not been able yet to extract them in sufficient quantities for therapeutic use.

As noted above, adult stem cells (and those from fetuses of more than 12 weeks gestation) have immune-triggering HLA surface proteins. Thus, while some advocate therapeutic use of stem cells derived from cord blood, adult bone marrow or the blood stream, these sources pose the problem of possible rejection reactions. Therefore, stem cells derived from these sources may have therapeutic potential only when given to the individual from whom they were derived (“autologous” transplantation) or from an immunologically matched donor (“allogenic” transplantation).

IRM Stem Cells

The Institute for Regenerative Medicine currently uses fetal liver cell (FLC) and fetal neuronal cell (FNC) stem cells from voluntarily aborted fetuses of five to 12 weeks gestation (IRM is also exploring the potential use of adult stem cells and cord blood stem cells). Fetal liver tissue has been shown to be a rich source of stem cells.^{9,10,11} As described above, recommended procedures are followed to maintain separation of the abortion decision from the donation decision, and to preserve confidentiality between donor and recipient. IRM FLC and FNC stem cells are purified and prepared using proprietary, patented procedures.

Therapeutic Use of Stem Cells: Theoretical Basis

Most diseases and disorders are caused by or at least involve damaged body tissues and insufficient repair. For example:

- Cancer chemotherapy and radiation therapy destroy many other non-cancerous cells in the body, including those of the bloodstream and immune system

- Hematopoietic disorders involve abnormal growth and/or destruction of certain types of blood cells
- Heart failure, generally regarded as incurable, involves damage to heart muscle, which the body cannot repair
- Liver failure involves progressive destruction of liver cells
- Stroke involves damage and/or death of brain cells resulting from a lack of oxygen and nutrient-carrying blood
- Type 2 diabetes, the most common form of the disorder, involves a progressive decrease in the body's ability to use insulin and to produce the hormone; its complications are due to progressive destruction of tissues in the eye (diabetic retinopathy, which can lead to blindness), kidney (diabetic nephropathy, which can lead to kidney failure), and nerves (diabetic neuropathy, which can lead to decreased sensation in the limbs and limb amputation)
- Osteoarthritis involves destruction of cartilage tissue around joints
- Parkinson's disease, Alzheimer's disease and other central nervous system disorders involve destruction of certain neurons in the brain
- Various autoimmune disorders involve immune system attack and destruction of the lining around nerves (multiple sclerosis), the cells lining the intestine (ulcerative colitis), cartilage in joints (rheumatoid arthritis), and other specific tissues for specific diseases
- Spinal cord injuries involve trauma and destruction of nerve tissue in the spinal cord
- Aging involves a general deterioration of the body's tissues

Stem cell therapy offers the potential to help repair and renew the damaged tissues associated with these and other diseases and disorders. Some of these specific diseases and experiences in treating them with IRM stem cell therapy are described below.

Fetal Stem Cell Therapy: Reports and Experience

The studies described below are largely based on data from the Ukraine and focus on the type of stem cell therapy (FLC and FNC) used by IRM. The descriptions are primarily clinical studies, (i.e., little to no data from preclinical [animal] research).

Collective Findings

In 2004, the Institute for Cryobiology and Cryomedicine in the Ukraine gathered data on the use of FLC and FNC therapy for treatment of more than 1700 patients suffering from a wide variety of diseases and conditions, including blood and immune disorders, diabetes, eye disorders (e.g., diabetic retinopathy, macular degeneration), neurologic conditions (e.g., spinal cord injuries, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis, and others), hemosuppression due to chemotherapy or radiation therapy for various types of cancer, gynecologic problems, chronic fatigue syndrome, gastrointestinal disorders (e.g., ulcerative colitis, Chron's disease, and abdominal adhesions), and others. As can be seen in the table, the various diseases generally responded well. Overall, there were "significant" improvements in 68%, partial improvements in 28%, and no improvement in 4%. The follow-up periods were up to eight years.¹² Other reviews of the Institute's experience in treating a wide range of patients with various cell preparations note positive responses in about 70% to 80% of patients.¹³

Table: Summary of Clinical Experience with Fetal Stem Cell Therapy, Institute for Cryobiology and Cryomedicine, Ukraine

Diseases	Number of Patients	Treatment Results: Degree of Improvement			Duration of Observation
		Significant	Partial	None	
Acquired aplastic anemia	18	14	2	2	1-8 years
Secondary anemic states	246	230	16	0	6 mos – 6 years
Thrombocytopenia	38	19	8	11	3 mos – 5 years
Diabetes	222	0	206	16	1-8 years
Diabetes retinopathy	230	194	36	0	1-5 years
Macular degeneration	86	74	10	2	1-7 years
Cytostatic disease (hemosuppression after chemotherapy and/or radiation therapy)	118	94	18	6	1-7 years
Gynecological pathologies					
- Endometriosis	12	10	2	0	1-5 years
- Septic complications	16	12	4	0	short term
- Anemia during pregnancy	39	39	0	0	short term
Neurology					
- Spinal cord trauma	16	0	14	2	1 - 5 years
- Nervalis fascialis	7	4	0	0	1 year
- Parkinson's disease	19	13	6	0	3 years
- MS	23	16	5	2	1 - 3 years
- Trigeminal neuralgia	46	46	0	0	1 year
- Cerebral palsy	13	0	13	0	9 mos - 4 years
- Amyotrophic lateral sclerosis	11	0	11	0	3 years
- Duchenne's disease	80	0	80	0	1 year
Multiple organ trauma	8	8	0	0	short term
Chronic fatigue syndrome	32	30	2	0	1-5 years
Arthritis	29	22	7	0	1-5 years
Psoriasis	12	9	2	1	1-8 years
Rejuvenescence (anti-aging)	139	120	19	0	1-7 years
Sexual pathology	88	52	22	14	1-8 years
Ulcerative colitis/Chron's disease	28	14	8	6	1-5 years
Abdominal adhesions	24	21	3	0	short term
Aesthetic application	140	140	0	0	1-5 years
Totals	1740	1181	494	62	
Percents	100%	68%	28%	4%	

Note: "Degree of improvement" generally refers to changes in one or more key clinical indicators of patients' disease status, as assessed by the treating physician(s). "Significant" improvement means a marked improvement in disease status and/or normalization or one or more disease indicators. "Partial" improvement means the progression of the disease was halted, as reflected by the clinical indicators.

Blood and Immune System Disorders

The western medical literature contains some reports of clinical applications of fetal stem cells in certain therapeutic areas. In particular, researchers in India and Europe have used FLC therapy to treat a variety of hematologic, immune deficiency, genetic and metabolic disorders (e.g., aplastic anemia, acute myelogenous leukemia, severe combined immunodeficiency, thalassemia, Fabry disease, Gaucher disease, Niemann-Pick disease),^{14,15,16} even to treat infants in the womb and shortly after birth.^{17,18}

These western literature reports are mirrored by case reports from the Ukraine of successful treatment of aplastic anemia with FLC therapy¹⁹ (see table also). Other reports from the Institute in the Ukraine show that FLCs have been used successfully to restore red blood cells, white blood cells and platelets in women after labor who acquire sepsis (a potentially life-threatening infection in the bloodstream) accompanied with anemia (response seen in 12 days), and in pregnant women with anemia.²⁰

Cancer

Cancer is typically treated with surgery and/or chemotherapy and radiation therapy. These latter two forms of treatment destroy cancer cells, but destroy other non-cancerous cells in the body as well – including red blood cells, white blood cells and platelets. Indeed, when levels of these essential blood cells are reduced below a critical level, chemotherapy must be reduced or suspended to avoid dangerous side effects, such as life-threatening infections, severe fatigue, and depression.

These three main types of blood cells are made primarily in the bone marrow from multipotent hematopoietic stem cells; thus, FLC therapy would seem a very logical and promising supportive treatment for patients undergoing chemotherapy or radiation therapy. By helping regenerate these blood cell families, chemotherapy could continue for its full course, often at even higher doses, which can significantly improve the prognosis. Supporting this idea is the data described above in which FLC therapy has been used to treat blood and immune system cancers and other disorders, helping to reconstitute normal blood and immune cell production. Data from the Institute also shows FLC therapy provides good hematopoietic support to patients undergoing cancer therapies (see table, “cytostatic disease”).

Professor Baltaytis and his colleagues have used FLC therapy for years as supportive treatment before and during cancer chemotherapy, and improved outcomes for many cancer patients. In addition, the impact of FLC supportive therapy during cancer treatment may go beyond hematological support. For example, one published report from the Ukraine showed that in 20 patients with pancreatic cancer, known to be extremely difficult to treat, administration of FLCs in conjunction with standard treatment, compared to standard treatment alone, significantly improved patients’ self-reported quality of life and decreased their fatigue.²¹

Disorders of the Spine and Central Nervous System

Ukrainian data on use of FNC therapy to treat spine and CNS disorders cover a wide range of therapeutic applications. We include results of treatment of some eye disorders as well in this section.

One published study noted improvement in 16 human patients with spinal cord injuries who were given FNC therapy six months to eight years after the trauma.²² Another included findings from three patients treated with FNCs within two months of having a stroke. The damaged area of the brain -- 3 cm or more, in the basal ganglia – was the result of blocked blood flow. FNC therapy was administered into the damaged area, guided by brain scans (e.g., MRI or CT scans). Six months after treatment, patients demonstrated improvements in verbal communications, motor skills and emotional states. Specifically, on the 100-point Orgogozo stroke scale, where 100 is normal, the average score was 25 before treatment and 70 afterwards. These positive effects continued for the 1.5 to 2 years of follow-up in the study.²³

Epileptiform (or trigeminal) neuralgia is a condition characterized by recurrent episodes of excruciating pain lasting several seconds or longer in face or head region, and is usually treated with anticonvulsant drugs. In one study, FNCs or a standard treatment were administered to 46 patients. Within 4-6 days, those receiving FNCs experienced reduced pain intensity, frequency and duration. After one year, the neuralgia completely disappeared in nine patients, and improved considerably in the rest.²⁴

A report from the Institute for Cryobiology and Cryomedicine in the Ukraine showed that, in 80 children with Duchenne's disease, a form of muscular dystrophy that usually begins around age six years, FLCs and other progenitor cell preparations provided partial improvement in muscular tension, rigidity, spasms, and sleep and speech patterns.²⁵ Another report from the Institute showed that, since 1998, FNCs have been used to treat patients with Parkinson's disease. Results on 19 patients, aged from 43 to 74, showed that six months after transplantation 20% achieved a "very good" response, 50% a "good" response, and 30% a "satisfactory" response.²⁶

A group of researchers in the Ukraine have developed a method for treating eye diseases by administration of FNC therapy behind the eye (parabulbar), and reported results in 38 patients with forms of retinitis pigmentosa. Visual acuity improved in 76.9%, and total visual field increased in 84.6%. Other electrical measures improved as well. The greatest improvements were found in patients with earlier stages of the disease; those with more advanced, late-stage disease did not improve significantly.²⁷

Additional data from the Institute shows that FNC therapy produced complete and partial responses in a variety of neurologic and visual disorders (see table). Professor Baltaytis and his colleagues have used FNCs to treat many neurologic disorders. In such cases, various stem cell suspensions were administered by means of intravenous infusion or implantation directly to the lesion. While the treatment produced positive effects, it takes a rather long time to work and, in many cases, additional courses of treatment were required, especially if the individual had the disorder for a long time. In treating spinal cord injuries, the treatment increased patients' sensation and movement, and improved bladder and rectal control. The outcome of treatment depends greatly on the timing of its initiation – the sooner FNC therapy is applied, the better the results and the prognosis.

Diabetes

Diabetes is currently one of the most widespread diseases, and its prevalence is rapidly growing around the world. Most of this increase is due to the rising prevalence of type 2 diabetes, a disorder associated with obesity and in which the body becomes insensitive to and less able to produce insulin, a hormone made in the pancreas and needed to transport glucose from the

bloodstream into body tissues.²⁸ In type 1 diabetes, which is much less prevalent than type 2, the pancreas is incapable of producing insulin entirely. In both forms of diabetes, unless treated, blood sugar rises uncontrollably, and over time can lead to such complications as cardiovascular disease, kidney disease (diabetic nephropathy), circulatory problems that may require limb amputation, vision loss and blindness (diabetic retinopathy), and nerve damage (diabetic neuropathy).

In a three-year clinical study, FLC stem cell therapy was administered at entry and at 12, 24 and 36 months to 29 people with type 2 diabetes. Beginning at six months after the first treatment and continuing for the three years of the study, measures of blood sugar control and blood lipids (such as cholesterol) improved significantly, and insulin medication requirements were reduced. Most interestingly, the number of patients suffering from diabetic retinopathy and diabetic neuropathy decreased dramatically from the start of the study to the end at three years: from 27/29 to 10/29, and from 24/29 to 10/29, respectively. Additionally, four of 17 patients with diabetic nephropathy reversed its progression to an earlier stage.²⁹

Another published report from the Ukraine cites findings from a study in patients with type 1 diabetes given therapy with placental tissue preparations. 58 patients in the experimental group were given the placental tissue therapy and traditional treatment; another 23 patients in a control group were given only traditional therapy. After 12 months, the patients in the experimental group decreased their insulin requirements by 34.6%, compared to a 6.23% decrease in the control group. Improvement in clinical signs were also noted.³⁰ Additional data from the Institute shows that FLC therapy produced partial responses in 206 of 222 patients with diabetes over a span of 1 to 8 years, and good responses in patients with diabetic retinopathy (see table).

Liver Disease

Among diseases of the liver, hepatitis and liver cirrhosis are among the most difficult to treat. Hepatitis is an inflammation of the liver that is caused by various viruses and other factors. Over time, hepatitis seriously damages the liver and can eventually lead to hospitalization and even death. There are at least six different strains of the hepatitis virus, including hepatitis A, B, C, D, E and G. Hepatitis B and C are considered the most serious and common.

Unfortunately, the efficacy of even the most advanced current therapies for chronic viral hepatitis is still rather low. For example, current antiviral interferon therapies result in sustained elimination of the hepatitis C virus in patients 20 to 90 percent of the time, depending on the subtype of the virus and patient factors. Hepatitis C is associated with liver cirrhosis 40 percent of the time, liver cancer 65 percent of the time, and the need for liver transplantation 30 percent of the time. Sociomedical problems related to liver transplantation – currently the only treatment for patients at the terminal phase of illness – are well known. For example, because of the shortage of donated livers, over 50 percent of patients on the waiting list die while waiting for transplantation surgery.

Using laparoscopic methods, Professor Baltaytis and Professor M. Kuchev implanted stem cells into the livers of nine patients suffering from liver cirrhosis and waiting for a liver transplantation. The patients showed significant improvements in liver functioning, symptoms of liver insufficiency and quality of life. All the patients lived more than 14 months, allowing enough time to undergo a liver transplantation operation. Professor Baltaytis and colleagues also

found positive effects of FLC therapy in the treatment of hepatitis, liver cirrhosis and chronic alcoholism of patients at earlier stages of these diseases.³¹

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) includes Crohn's disease and ulcerative colitis. Chron's disease is a chronic inflammatory disease of the intestines. It primarily causes ulcerations (breaks in the lining) of the small and large intestines, but can affect the digestive system anywhere from the mouth to the anus. Ulcerative colitis is also a chronic inflammatory condition that involves only the colon.

The exact cause of IBD is unknown. Some scientists suspect it may be triggered by infections from certain bacteria; others believe it is an autoimmune disorder in which the immune system attacks the cells lining the digestive tract. Recent research suggest IBD may involve genetic predisposing factors.³²

Currently there is no medical cure for IBD, and current treatments are not very effective. Once the diseases begin, they tend to fluctuate between periods of inactivity (remission) and activity (relapse); the treatment goal is to promote longer periods of remission and reduce the frequency and duration of relapses. Current approaches include treatment, as necessary, with anti-inflammatory medications, immune suppressing agents, anti-diarrheal medications and/or other drugs. Dietary modifications, such as reducing fiber intake and consuming a liquid diet, can be helpful. If portions of the intestine become severely diseased, surgery may be required.³³

Because IBD involves immune system destruction of cells in the intestine, stem cells therapy has the potential to help treat the disease by regenerating some of the destroyed tissue and/or favorably modulating the immune system so it is less prone to attacking the intestinal cells. Data from the Institute for Cryobiology and Cryomedicine showed good responses in a majority of patients with ulcerative colitis, Chron's disease, or another disorder, intestinal adhesions (see Table).

Arthritis

There are two major types of arthritis: rheumatoid arthritis and osteoarthritis. Among the over 100 different types of arthritis conditions, Osteoarthritis (OA) is the most common.³⁴ OA is caused by the age-associated breakdown and eventual loss of the cartilage "cushion" of one or more joints, leading to pain and limitation of joint mobility. Inflammation of the cartilage can also stimulate new bone outgrowths (spurs) to form around the joints.³⁵

Less common, rheumatoid arthritis (RA) involves inflammation in the lining of the joints and/or other internal organs, and typically affects many different joints. It is usually chronic, and can have flare-ups. The inflamed joint lining, the synovium, can invade and damage bone and cartilage. Inflammatory cells release enzymes that may digest bone and cartilage. The involved joint can lose its shape and alignment, resulting in pain and loss of movement. The cause of RA is not yet known, but it is recognized as an autoimmune disease.³⁶

Because both forms of arthritis involve destruction of cartilage around joints, stem cells therapy has the potential to help treat the disease by restoring some of the lost cartilage. Only initial data from the Ukraine support this: all of 29 patients given FLC therapy had responses (see Table).

Action Against Effects of Aging

Aging is a complex process, and its causes are not completely understood. However, regardless of the exact mechanisms involved in aging, one thing is certain: cells become progressively damaged over time and die. Thus, replacing aging cells with new ones, as with stem cell therapy, holds promise.

There is only limited evidence of an “anti-aging” effect of fetal stem cells reported in the medical literature. In one report, fetal liver cell and cord blood stem cell preparations improved immune function and hormonal balance in patients undergoing cosmetic procedures, and thereby enhanced the cosmetic outcome.³⁷

Indirect evidence, however, suggests fetal stem cell therapy may be associated with improvements consistent with an “anti-aging” effect. Indeed, data from the Ukraine shows that all patients given fetal cell anti-aging therapy reported a rejuvenating effect (see Table). In more than 20 years of administering such therapy to people suffering from a wide range of disorders, Professor Baltaytis and his colleagues noticed patients consistently reported – often unsolicited – intriguing anti-aging “side effects” of the treatment. The specific effects differed according to each individual’s age and health status, but some reported by patients included:

- Various effects leading to improved fitness, including increased feelings of energy, vigor and inner strength; improved mobility, coordination, strength and endurance; and increased desire for physical activity
- Improved joint function and reduced symptoms of arthritis
- Improved mental capacity, concentration and ability to maintain attention; increased clarity of thinking, speech and memory
- Improved psychological state, including elevated mood and positive attitude; decreased irritability, sleepiness and apathy
- Improved sleeping pattern, with decreased insomnia and other sleep disturbances, and feelings of being refreshed upon awakening
- Restored activity of impaired and damaged internal organs and tissues
- Normalized production of red and white blood cells and improved immune function
- Enhanced sexual function
- Improved appetite

Others have reported more unusual effects, such as improved hearing and color perception. Finally, some effects may not be immediately obvious, since changes take place on the cellular level.

Safety

Safety is always a concern with any therapy. Data from the Institute of Cryobiology and Cryomedicine in the Ukraine show no serious adverse effects in any of the total 2925 patients given fetal cell therapy since 1986 and followed for one to the maximum of ten years. In rare instances, patients experience brief, transitory reactions such as swelling and redness near the infusion site, rash, or dizziness, but such effects soon resolve.

It is important to note, however, that stem cells are biological materials and, just as with blood transfusions and organ transplantations, they carry a very small potential risk of transmitting known or unknown pathogens. To minimize such risk, rigorous standard screening tests are performed on both the donor and the stem cells, similar to tests used with blood donations. IRM

also follows safety screening, testing and preparation procedures according to standard requirements of tissue banks. To further ensure safety, IRM employs additional procedures, exceeding usual testing standards, that use the most current technologies such as PCR (polymerase chain reaction) to detect pathogens, even if present in extremely minute quantities.

One of the key concerns about embryonic stem cells is that, because they constitute such early progenitor cells (derived from a blastocyst, the ball of cells that forms 5-6 days after an egg is fertilized), they have a greater potential to grow uncontrollably, for example into a type of tumor called a teratoma.³⁸ However, the stem cells used by IRM, as noted above, are derived from elective abortions of fetuses six to 12 weeks gestation, and are therefore more “mature” than primitive blastocysts. The Institute for Cryobiology and Cryomedicine found no cases of teratoma in any of the total 2925 patients given fetal cell therapy since 1986 and followed for one to the maximum of ten years.

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