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For Kids' Sake

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A Support Network Helping Children With Scleroderma & Their Families Spring 2005

Stem Cell Transplantation In Juvenile Systemic Sclerosis

Written by, Ronald M. Laxer, MD, FRCPC
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Dr. Ronald Laxer also serves on the JSDN Medical Advisory Board.

The treatment of juvenile systemic sclerosis has not been one of medicine's major areas of success, as opposed to that of many other rheumatic diseases. While rheumatologists have become better at treating many of the symptoms associated with juvenile systemic sclerosis (e.g. reflux, Raynaud's phenomenon), many treatments aimed at the basic mechanisms leading to the sclerodermatous process have not been proven to be effective. Examples include corticosteroids, cyclosporine, Interferon, relaxin and penicillamine. Methotrexate and penicillamine have both been studied in randomized trials, and neither have proven definitively to be effective. Nevertheless, both penicillamine and methotrexate continue to be used for some patients, perhaps with limited success.

Because of the severity of some cases of juvenile systemic sclerosis and the lack of proven effective treatment, new approaches to the treatment of juvenile systemic sclerosis have been developed. One of these new methods is called High Dose Immunotherapy with Stem Cell Rescue (also known as Stem Cell Transplant), a form of treatment which has proven to be effective in some forms of cancer in adults as well as in children. The rationale behind this treatment is as follows: the scleroderma process is set in motion by the body's immune system, which for some reason has escaped normal control mechanisms and proceeds to stimulate cells to make excessive amounts of collagen which get deposited in the skin, blood vessels and many vital organs such as the lungs, heart, kidneys and gastrointestinal tract, leading to progressive "scarring" of these organs. If these "out of control" cells could be removed from the body before too much damage has occurred, then the scleroderma process might be able to be kept in check.

The basic mechanism behind the process of High Dose Immunotherapy with Stem Cell Rescue is that stem cells, the originators of cells that lead to blood forming and immune cells, are taken from the patient and stored (harvested). Patients are then treated with high doses of chemotherapy and the immune system and blood forming elements are essentially wiped out. This serves the purpose of getting rid of the immune cell(s) which may have initially triggered the scleroderma process. The patient's stored stem cells are them given back to the patient intravenously, and the body's immune system and blood-forming cells are then "put back together", or reconstituted. This is a very intensive process, which may be somewhat risky for patients, especially when their blood counts are very low, as they are at a higher risk of infection. It must be performed under very controlled situations and in centers with extensive experience with such procedures.

This treatment has been used in probably fewer than 100 adults with severe systemic sclerosis, and in only a handful of children. It is important to time the treatment appropriately. To be effective, it must be done before irreversible organ damage has taken place. On the other hand, it must not be done too early, as one would not want to use such an aggressive therapy in a patient whose ultimate course is not known, as the treatment may be worse than the disease. Therefore, it is very important to have predictive factors as to the ultimate outcome, and while there are some in adults with scleroderma, this area has not been studied in children.

The short-term results with High Dose Immunotherapy with Stem Cell Rescue in adults appear to be promising. However, the very long term outcomes are still not available, and some patients, despite initial improvement, have had a relapse. Several children have been treated with this approach, with success in a few.

For patients with progressive juvenile systemic sclerosis and no other therapeutic options, this does appear to be a valid and rational approach to the treatment. Protocols are underway for children with rheumatic diseases.♥

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A Message From the Board Of Directors

As we reach our sixth year anniversary it is a perfect time for reviewing the past and planning for the future. As board members we are indeed proud of the difference the JSDN has made in the lives of juvenile scleroderma families over the years.

Each and everyday our backyard expands into different towns and new areas of the healthcare community world-wide.

The JSDN has focused much attention on expanding the outreach programs from year to year. We concentrated our efforts over the latter half of this year on improving the infrastructure of our organization to ensure its viability for years to come. Many of these improvements have been behind the scenes, including the design and launch of our new website, improved budgetary planning and tracking methods, plans for broader fundraising efforts, and a more structured volunteer program.

Whether you have been a financial supporter of the JSDN, a volunteer, or even a supporter in conversation your contribution makes the JSDN work. Thank you for your support.

But today, more than ever before, the not-for-profit sector is being asked to do more with less. We need your financial help to build the future and ensure that the juvenile scleroderma families are met. We invite and welcome your support.♥

It takes a nation to bring an organization together…

Warm Hugs & Support,
Kathy ♥ Jerry ♥ Carmela ♥ Sherry ♥ Roxanne

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***P**rovides membership packets with valuable information*
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***P**rovides a JSD Database*
***C**onnects families to a support network for children with juvenile scleroderma*

Whatever you are going through - there are others who have walked the path or walking through it now - and can help you…Remember you are not alone!

The Doctor's In: Q & A

Thomas J.A. Lehman, M.D. Chief, Division of Pediatric Rheumatology at the Hospital for Special Surgery in New York City, and Professor of Clinical Pediatrics, Cornell University Medical College.
Dr. Lehman serves on the JSDN Medical Advisory Board.

Q: ***My sister has scleroderma and always has cold hands and feet. Is there anything I can do about this?***

A: *Cold hands and feet are a very common problem for children with scleroderma. In many cases they look pink or a little bluish and always feel cold to the touch. The child is often not uncomfortable and does not complain of numbness or other problems with the fingers. These children should be advised to dress warmly including gloves, but their cold fingers are mostly just annoying. Other children have Raynaud's phenonmenon. This is different because the fingers turn white and get numb. Often it is only a part of one or several fingers, but it can be the whole finger. Because turning white and getting numb means there is no blood flow this is a much more serious problem. Children with scleroderma who have white, numb fingers should immediately go inside and warm up their fingers (often the most convenient thing is to simply sit on them). Don't use hot water or things like that because you can burn the fingers. If the fingers don't turn back to normal and are still white and numb after 30 minutes the child should seek medical care. If the fingers are white and numb for too long there could be permanent damage. Children who have this problem frequently may need to take medicine for it.*

Q: ***My 7 year old son was diagnosed with linear scleroderma by one doctor and morphea by another. What does this mean? Will he get internal organ involvement like some people with scleroderma I've heard about on the internet?***

A: *There are many children with localized scleroderma which only involves the skin and the tissues right under it. Oval lesions are often called morphea while lesions that appear to be in streaks are typically called linear scleroderma. Physicians who don't specialize in scleroderma often use the terms interchangeably. It's not a major concern because the two conditions seem to blend into each other. Since we treat them the same way, the distinction isn't very important. What is important is whether or not the lesions are crossing a joint and likely to cause growth or movement problems.*

Many parents are concerned that their children with localized scleroderma (morphea or linear scleroderma) may develop internal organ involvement and have "full fledged scleroderma = progressive systemic sclerosis." I've followed many many children with all these diseases. Although I hear about children with localized disease who developed internal organ involvement, I've never seen one. I've read many of the reports and remain skeptical. If this happens it is very very rare. If you have a careful doctor watching your child they will notice if any internal organ involvement occurs and take the necessary steps. It isn't likely to happen.

Q: ***My child has scleroderma. Is she getting the right medicine?***

A: *This is a common question, but of course it can only be answered by a physician who has seen and cared for the child. I can answer lots of general questions for people, but I can't answer specific questions about your child because I've never seen them and don't know all the appropriate details.*♥

The Doctor's In: Q & A: Do you have a medical question that you would like answered? We'd love to hear from you. Questions may be edited for brevity. We regret that we cannot answer medical questions personally, but do offer a pediatric rheumatology referral list to those seeking specific diagnosis. **Please send to:**
JSDN – Q & A, 1204 West 13th Street, San Pedro, CA 90731 or email KathyG@jsdn.org.

Lung Involvement In Childhood Scleroderma

Written by, Terry L. Moore, M.D., F.A.C.P., F.A.A.P, F.A.C.R.
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Dr. Terry Moore serves on the Juvenile Scleroderma Network's Medical Advisory Board.

It is estimated that approximately 3% of all patients with scleroderma are children. Children under 10 years account for less than 2% of all cases. The patients between 10-20 years make up from 1.2% to 9% depending on the study involved (1). In the children with childhood scleroderma, lung involvement occurs in quite a high percentage of patients. Lung involvement many cause the most mortality now in scleroderma. Of those who die with scleroderma, 50% die of pulmonary hypertension (PHT) and 25% with pulmonary fibrosis (2). Pulmonary disease usually involves either pulmonary blood vessels and tissue including predominantly interstitial fibrosis with gradual obliteration of the blood vessels, combined pulmonary tissue and vascular lesions, or predominant pulmonary blood vessel involvement associated with rapidly lethal right ventricular failure. Pulmonary disease is almost universal in diffuse scleroderma, although frequently asymptomatic. Symptoms may not occur until 60% of the pulmonary function is compromised. The patients often have a dry, hacking cough or shortness of breath on exertion. Occasionally, rales or pleural friction rub are present on examination (1). The main histological abnormality in the lungs is diffuse alveolar, interstitial, and peribronchial fibrosis. The thickened walls may result in reduction of alveolar space. Extensive bronchiolar hyperplasia, arteriolar endothelial proliferation, fibrous pleuritis, and pleural adhesions are also present (1).

Initial evaluation of a child for possible childhood scleroderma and lung involvement should include a complete blood count (CBC), urinalysis, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), comprehensive metabolic panel to measure liver and kidney function tests and muscle enzymes (CPK and aldolase). Immunologic studies should include a rheumatoid factor, antinuclear antibody (ANA) looking for a speckled, nucleolar, or centromere pattern on immunofluorescence, and specific antibodies for DNA topoisomerase-1 (anti-Scl 70 antibody) or centromere. If available, testing for antibodies to PM-Scl and RNA polymerase III may be indicated. The presence of these antibodies indicate a greater possibility of lung involvement. The original evaluation of the child will also include pulmonary function tests (PFTs), echocardiogram, and high resolution computerized tomography (CT) of the lung. Pulmonary diffusion and spirometry are sensitive measures if restrictive changes are present in the respiratory tract in childhood scleroderma. If restrictive changes are present, characteristic findings include a decrease in the forced vital capacity (FVC) and forced expiratory flow, an early decrease in diffusion capacity (DLCO), and an increase in functional residual volume (3, 4). A two-dimensional echocardiogram is important in confirming early PHT by documentation of a dilated right ventricle with thickening of the ventricular wall and straightening of the septum, and measuring right ventricular pressure. The one-dimensional M-mode echocardiogram is characterized by changes in the mid-systolic movement of the pulmonary valve. Right heart catheterization provides definitive confirmation of PHT (1). High-resolution CT of the lungs may give more involved information in evaluating the patient with childhood scleroderma.

Interstitial fibrosis of the lung in childhood scleroderma is a severe, fibrotic process without a lot of involvement in the blood vessels. The way to determine if inflammation of the breathing sacs of the lung (alveolitis) is present is the high-resolution CT scan (2). A bibasilar, peripheral, ground-glass appearance on the CT scan correlates very nicely with progression of fibrosis, changes in PFTs, and also with improvement after treatment. The patients with antibodies to Scl-70 (topoisomerase) or nucleolar pattern on their ANA have a high risk of developing pulmonary fibrosis. To determine if significant alveolitis should be treated, a combination of potential findings including a decrease in FVC, a 10% decrease in DLCO, and a ground-glass appearance on high-resolution CT should be noted. Dr. Steen's studies (2) have shown only the use of cyclophosphamide had significant improvement in these patients over a two-year period with stabilization and improvement of their FVC. Another possible drug that may be helpful is that of bosentan, an endothelin-1 antagonist. Endothelin is a profibrotic peptide and possibly bosentan will prevent further development of fibrosis.

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Pulmonary vascular disease in scleroderma can be a very lethal complication. Blood vessels show diffuse intimal proliferation with occlusion of lung vessels similar to narrowing of the digital blood vessels (2). Severe PHT is unrelated to severe fibrosis. The patients with PHT have minimal fibrosis or restrictive disease with an FVC of 80% predicted similar to the patients without PHT. However, at the time of diagnosis, the DLCO may be very low. The risk factors for isolated PHT include long duration of Raynaud's, limited scleroderma, and the presence of anticentromere antibodies (2). The patients with PHT tend to have a high frequency of pericardial effusions including tamponade (5). Pulmonary systolic pressure on echocardiogram higher than 35 mm Hg is compatible with early PHT. However, interpreting the significance of the level of pulmonary artery pressure sometimes has problems with echocardiograms as a screening tool (2). The physician specifically needs to request to measure pulmonary artery pressures. To confirm PHT, a right heart catheterization may need to be performed. If the pressure is greater than 45 mmHg, there is a 90% correlation with the right heart catheterization. The patients with longstanding disease, anticentromere antibody, low DLCO, and a pulmonary artery pressure greater than 40 mm Hg are suspect for PHT. The patients with primary PHT sometimes have a positive response to nitric oxide, a short-acting inhaled vasodilator (6). This may indicate a possible good response to high-dose calcium channel blockers, such as nifedipine. However, childhood scleroderma patients may have low systemic blood pressures and usually cannot tolerate these medications because of dizziness and hypotension as side effects. Newer treatments such as epoprostenol, bosentan, and treprostinil sodium have now been approved for PHT in both primary and scleroderma PHT (2). The problem with epoprostenol is that it is a continuous intravenous effusion, which has many complications and is extremely expensive. Treprostinil, a continuous subcutaneous infusion, has some side effects such has nausea, headache, and jaw pain, and a very painful local site reaction that occurs in 85% of the patients, and is also extremely expensive. Bosentan, the endothelin antagonist, is an oral agent, well-tolerated, and is a very potent vasoconstrictor. It decreases pulmonary artery pressures and improves right ventricular mass. Increased liver function tests are the main complication and monthly laboratory tests are required.

Lung disease is very common in childhood scleroderma. It is a very serious disease and requires a careful evaluation of risk factors, laboratory studies, PFTs with DLCO, high-resolution CT scans, and echocardiograms to determine the primary type of lung disease and the most appropriate treatment.♥

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On behalf of the children with juvenile scleroderma, thank you for shopping at the JSDN online store ☺

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A Personal Look At Juvenile Scleroderma

Written by, Cathy, Amber's Mom

Amber is a 15 year old teenager who wants to hang out at the malls with friends. She has a whole new interest in music, clothing, makeup and boys. She wants to be in school everyday talking and chatting with her school mates. There is only one thing wrong Amber is sick with MCTD. She is a teen trapped in an 70 year old body. Her knees, hands, back, arms and ankles are always in pain from arthritis. Her eyes and skin can not handle the sun. Her teeth are yellowing and gums are receding. She can't walk 10 steps without losing her breath, her skin is so tight on her hands that her fingers are curling, her legs hurt because of thickening of the skin.

For the last three years her doctors have been trying to get Amber's illness under control. They have been able to slow down the progression a little. Unfortunately the illness was misdiagnosed for five years, leaving severe scarring in Amber's lungs. All of this damage is irreversible.

Amber sees so many doctors that our friends and family can no longer keep up. Her list of medications is longer than both her grandparents put together. Some of Amber's medications are hard to deal with emotionally as well as physically. Pulse Cyclophosphamide was becoming too toxic for her, putting her in the hospital every month. Prednisone, the drug Amber hates very much, caused her face to swell up to where it would hurt, and it became hard for her to wear shoes. If three years of Prednisone wasn't bad enough, the doctor added bi-weekly pulse steroids. This medication made her hurt so much they had to give her liquid codeine every four hours. She has so many others to take as well. Amber has experienced many different emotions from anxiety, sadness, fear, and rage. She takes medication for depression and has a wonderful counselor that has helped her learn to deal with her emotions.

We have agreed to send all data to a central registry and to share all info that may be helpful for other children like Amber.

Earlier this year her pediatric rheumatologist told us about stem cell transplant. He said we needed to do it as quickly as possible so that we could maintain what quality of life Amber has left. He also told us the only other option would be for Amber to go on a transplant list for a lung and heart transplant. This scared me so much to hear this. He sent us to an adult rheumatologist who specializes in scleroderma, and has also done the stem cell transplant on a patient who is going on three years in remission. This gave both Amber and I hope. We talked and both agreed that the stem cell transplant was what we would try next.

We were very nervous and scared but if it worked the doors of the world would open for Amber. If not, well, we would deal with whatever happened. What I did know was that without this treatment there was nothing that would stop this illness from taking over Amber's lungs and heart. There is a 50/50 chance this will show some kind of improvement. It can be temporary. If improvement is seen for two years, odds are it will continue to get better. I like the 50/50 chance better then watching her go through this illness.

We were told she would be in and out of the hospital for four weeks before the transplant, five weeks in hospital, and four weeks after as an outpatient. Amber would be in a sterile environment. To lower her immune system they would use cyclophosphamide. She would also be on Neupogen (G-CSF) to help make the stem cell counts go up, and Thymoglobulin to destroy T-cells. The biggest danger would be infection. For her own protection Amber would be in isolation. During the procedure she would also be on medications to help prevent certain viruses. After Amber's procedure she would remain on many medications to help prevent lung infections.

On February 21, 2005 we followed the procedure with a few minor differences. Amber only needed the G-CSF for three days instead of the anticipated 2 weeks. Her white blood count went from 0.8 to 28, the norm being 4.0-11.0. She lost all of her hair. She was very sad and upset about that. But I made a game of it. We had fun using the hair for beards and moustaches and boy did we ever laugh.

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When they harvested the stem cells it was truly amazing. I watched the machine at work. It took the blood from Amber, sent it through a lot of tubing into the machine, which spun it and every now and then harvested the stem cells and hemoglobin. You could actually see the stem cells separate. It was amazing.

When that was done they began killing her old immune system. They used large doses of chemo and a drug called thymoglobulin. This is a very harsh drug and it gave Amber a lot of breathing problems. They also gave her a mixture of meds that are used on all bone marrow and stem cell transplants. Amber was beaten up from the inside after 3 days of meds and an extra day of chemo.

They had to stop the naproxen for Amber's arthritis and put her on morphine because Amber's platelets were too low. They had to give her a few blood transfusions to bring up her platelets, and she looked good after that. Her oxygen saturations came up to a 100%, something that has never happened before. This lasted for the day and her saturations went down into the 60's. They got her up to the 80's with oxygen. Man I was scared but always stayed strong for her and always insisted on her smiling everyday.

The day they gave Amber back her stem cells they called Day 0. The stem cells came in 3 huge syringes, which they gave thru IV. A few days later Amber started to get a fever and they started her on all the preventative meds. They checked her for fungus but it all came back fine. Amber's counts then dropped down. Well these did not stay down long and after that her counts climbed quite well.

They told us she would be in the hospital at least 4 weeks after the transplant. Well, did Amber ever prove them wrong! After only 13 days they were telling her she was ready to get out of the hospital! A few days for all the docs to see her and some tests and she was a somewhat free bird. Amber also decided to help research this new breathing test that will help eliminate having to get so many CT scans. Amber was a true trooper through this all and she smiled everyday. The big factor that got Amber out early was that she never stopped eating or drinking even though they were giving her TPN(nutrients vitamins and so on) and Lipids fatty food source. Now Amber's only jobs are to drink 2.5 liters a day and to get plenty of rest.

She is happy to be home and I know she'll have a much more speedy recovery here. She will be on Penicillin for 1 year and Septra for 6 months then she has to go and get immunized all over again but I am leery of that.

We have agreed to send all data to a central registry and to share all info that may be helpful for other children like Amber.

It was a journey and we flew through it in the clouds amongst all the prayers for those who care. My daughter Amber Mae Woods is a HERO. She fought a battle and she won. She is also my HERO and I am so proud to be her Mum.♥

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Please keep in mind, the JSDN programs and services would not be possible for families if it weren't for our generous donors and membership to the JSDN!

Without your generous help the JSDN will no longer exist! Many families rely on the JSDN for help.

The JSDN does not receive any money from other scleroderma and related diseases organizations.

There are many ways you can help the juvenile scleroderma cause…
Join the JSDN!
Make a donation!
Volunteer to raise awareness!

We greatly appreciate everything you can do for the JSDN and the juvenile scleroderma cause!

~JSDN

♥♥♥♥

Adults aren't the only one who get scleroderma!

Becoming a member to the JSDN connects people to a support network for children with JSD & their families. It is important to families to have a support network to exchange information and find emotional reassurance.

Yes! ***I want to join the JSDN. I understand this includes a one year <u>tax-deductible</u> membership to the JSDN.***

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The JSDN is a separate non-profit organization from all other scleroderma organizations. The JSDN does not receive funds from other scleroderma organizations. The JSDN depends on your membership and donations for the JSDN programs and services. Thank you!

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For Kids' Sake

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Mission Statement:

It is hard enough to face the effects of Juvenile Scleroderma, but facing them alone can be devastating. The Juvenile Scleroderma Network, Inc invites families nationwide to become involved and help provide support and friendship to children who have Juvenile Scleroderma.