



Mary Smith, President
John Harings, Treasurer
Cindy Remme, Secretary

**The Carol Ann Foundation &
International Morquio Organization**

8164 W. Circulo De Los Morteros
Tucson, Arizona 85743

Telephone: 520 744-2531 Fax: 520 744-2535

E-mail: mbs85705@yahoo.com Web site: morquio.com

Morquio News 22

May 5, 2008

RE: MPS IVA (Morquio) Project

Dear ALL Morquio Families and Friends,

We hope that all Morquio families are doing well. First of all, thanks for everyone's great contribution on the Morquio Project. We highly appreciate having all Morquio families join our movement and activity. At present we have around 380 patients enrolled in our international registry from over 40 countries. This is quite exceptional since Morquio A disease is very rare (1 out of 200,000 to 300,000 births and 1,200-1,500 patients in advanced countries).

Please kindly send the annual questionnaire since update information is critical and we can feedback to all Morquio families (please see attached the questionnaire. It is available on www.morquio.com as well). Also please keep the record of growth chart if you have. We are very close to have the clinical programs to be announced. Please be patient a little more. We will also distribute the growth chart of Morquio once professionally designed. Please also wait a little more.

Dr. Tomatsu and his Morquio Dream Team have also started to develop new therapeutic approaches on Morquio and MPS.

Brief summary of the Morquio Related issues is as follows.

We have two outstanding news from Japan.

Morquio Project started at Gifu University in Japan 25 years by Emeritus Professor T. Orii and a number of Japanese researchers contributed to this project for many years.

1. Muconet Japan (President Kotaro Tasaki: <http://www.muconet.jp/>)

Muconet Japan is very pleased to announce that The Foundation has granted the renewal (the 2nd year) of funding of \$5,000 for Dr. Adriana Montañó (starting on July 1, 2008) for a new therapeutic approach on Morquio. The Foundation will provide additional funding this academic year (2008-2009 year) depending upon the progress of Morquio Project.

E-mail: info@muconet.jp

Thanks for the great commitment on Morquio Project. We start a new Morquio Project with the precious funding (by Dr. T and Dr. M).

See part of activity by Muconet Japan below. Their activity is very broad from the concert, marathon, issue of the books, professional wrestling etc.



Live Concert 「Fist Up From Ciccoh ~ PRIDE OF CICCOH FOREVER」



March 23, Core Member (Nakai Family and her supporters) with Woman Professional wrestler (right picture, the far right)

2. Care for Sota Morquio Foundation

Care for Sota Morquio Foundation (Japan) raised the fund of \$5,000 for Morquio Project. Thanks for the precious funding for Morquio Project.

Care for Sota Morquio Foundation

Saori Isomoto

Website: <http://www1.ocn.ne.jp/~morquio/index2.html>

E-mail: saori-fanfan.i@docomo.ne.jp

Care for Sota Morquio Foundation has been established in Japan 2 years before and has been very active to promote Morquio Project. Care for Sota Morquio Foundation has a direct talk with Japanese Prime Minister and Health, Labor, and Welfare (HLW) Ministry

to promote Morquio Project in Japan. Japanese government appreciates the formidable efforts by the patient society and has promised to promote the early approval of the drug in Japan. The Japanese government also appreciate that Morquio Project started 25 years ago at Gifu University in Japan by Emeritus Professor T. Orii and Dr. T and is proud that many Japanese researchers greatly contributed to Morquio Project for many years. The government now has a serious concern on this project. This is an extraordinary commitment that Japanese Prime Minister meets the Morquio Family since Morquio Disease is such a very rare disease.



April 21, at Iwakuni Japan. Japanese Prime Minister, Mr. Y. Fukuda meets Souta Isomoto (8 years) and his mother and command to the HLW ministry to take care of promotion of Morquio Project in Japan (less than 100 patients in Japan).



April 24, Isomoto Family hands the signatures of the petition over to HLW Vice Minister, Ms. Nishikawa. Vice Minister appreciates the activity of Foundation and is proud that Morquio Project initiated in Japan and that many Japanese researchers have contributed to this project for a number of years.



At the front of LHW ministry with Isomoto family and Dr. T (after meeting of HLW ministry)



With Souta Isomoto

Thanks for Bennett Foundation, Waters family, and many volunteers!!! This is a huge effort to hold such a big event.

The coming events (meet Morquio families!)

1. Stephanie Bozarth

See web site!

Stephanie Bozarth

(703) 256-1980

Web: morquio.sagepointe.com/index.asp

Mad Hatter Tea party: 12:30- 4:00 PM June 1

Place: Stardust Restaurant & Lounge

608 Montgomery Street Alexandria, VA 22314

Annabelle's Website

<http://www.caringbridge.org/visit/belle>, <http://www.morquio.org>

**Mad Hatter Tea
Party**

Sunday, June 1, 2008 ~ 12:30 - 2:30 PM

Stardust Restaurant & Lounge

608 Montgomery Street

Alexandria, VA 22314

**Pat McGee Band &
Sister Hazel**

Friday, July 18, 2008

Wolftrap Filene Center

Vienna, VA

**Southern Living at
HOME Shopping
Benefit**

April ONLY

www.southernlivingathome.com/michellerogers

All Fundraising Efforts Coordinated by:

Stephanie & Austin Bozarth

Contact us: stephbozarth@yahoo.com



Annabelle Bozarth 17 months old

Morquio meeting and scientific events:

1. **LPA annual meeting at Detroit.**

We have Morquio Workshop on June 22nd from 1:30-2:30 PM. Dr. T will present update data on Morquio Project.

**2008 National LPA Conference
Detroit, Michigan
June 20th - June 28th, 2008
at the
Detroit Marriott
Renaissance Center
800-228-9290 toll-free
313-568-8000 direct
Join LPA!**

2. 10th International Symposium on Mucopolysaccharide and Related Diseases
Vancouver, Canada hosted by Canadian MPS Society. June 26-29

We will have a lot of presentations at the meeting.

3. Japanese MPS Society Meeting (Tokyo, Japan) August 22-23

4. 1st International Morquio Conference, UK August 29 – 30

We will announce to hold 1st International Morquio Conference at Manchester UK at August 29 and 30, 2008. UK MPS and Dr. T will organize the meeting. This is the 1st attempt to have all Morquio families internationally at one site. This conference is specific to Morquio syndrome (MPS IVA). We expect all families and experts together! As soon as we define the schedule, we will announce it. Please mark the date!
It will be a huge conference!

The other meetings: TBA in future

2. Annie and Mandy Bellassai Website

Bellassai Family are planning to connect among families and local communities through the internet!

Maurizio Bellassai and Betsy Bellassai

Website : www.bellassai.com/morquio

E-mail: Maurizio@bellassai.com

3. Jacob Randall Foundation for Morquio

Jacob Randall Foundation will hold the meeting next year as well at Tampa, FL.

President Renee Little

Telephone: 813- 731-8274

Website: www.jacobrandallfoundation.com

E-Mail: rjl197@verizon.net

We will have a discussion with an individual family at both family meetings.
The following issues will be presented and discussed.

1. International Morquio A Registry

2. Educational CD for Morquio
3. Murine models for MPS IVA
4. ERT of MPS IVA
5. Question and Answer

We are very pleased to meet as many as Morquio families through the meeting. We are very happy to make a presentation of our Morquio Project to date and to discuss with each individual family

We have the similar questions on Morquio A syndrome as follows:

Recent questions:

Q1. How can I tell my child is severe or mild? My affected child is similar to other Morquio kids?

Ans. I enclose the Morquio Registry paper here which over 300 patients have kindly contributed to through the questionnaire. You may see some similarity and difference with your kids. Clinical severity is sometimes difficult to say exactly: at least we must see the information of **growth chart**, **DNA analysis**, **enzyme assay**, and **keratan sulfate** level. We are very close to finish “Growth Chart for Morquio Patients” with age. Once it is available, you may compare your kid with other Morquio kids. We will inform you! **Please keep the growth chart record as many as possible since at birth.** We will also have more registry and biochemical data to be published. Thanks for your great contribution!

Q2. How important to measure keratan sulfate (KS)?

Ans. KS is sort of sugar chain. Morquio patients can not digest KS since one of the enzymes to digest KS is missing in the body. Therefore, KS is accumulated in the body, especially, in the cartilage (bone) and eye cornea. The stored KS will destroy the cartilage layer (growth plate). Because of that, Morquio patients have a lot of signs and symptoms related to the bone. It is quite important to know how much KS is elevated in the body (urine and blood). KS level is age-dependent and it is the highest when the kids grow. There are two major methods to measure KS quantitatively: one is to use antibody against KS and the other one is to use the very modern instrument (so-called, tandem mass spectrometry). Tandem mass spectrometry is very sensitive method and can measure KS even in the mouse.

Q3. When do we have to consider the surgical operation?

Ans. It is hard to predict when the appropriate time is. However, the most important operation is “cervical fusion” to protect against the unstable neck. From the registry data, around 30% of patients who had operations may require it. The average age is around 9 years. Please ask the experienced doctor about the indication.

Q4. Is there any animal model of Morquio? How will you confirm whether any treatment is effective or not prior to human patients?

Ans. So far except human patients we only have three different types of Morquio model mice. No other animal models are known. Generally, we try to treat the animal model prior to human patients. Since there is no animal model except mice, we use Morquio mouse model at this point. Our mouse model has a unique feature to produce inactive human Morquio enzyme. Therefore, we can treat this mouse model continuously for a long term without any problem. Generally, if we infuse the human enzyme into the mouse body, the human enzyme will be neutralized since the mouse recognizes it as a foreign body. We are treating Morquio mice by several different treatment methods to see

the effectiveness. The most important issue is how to reach the bone especially, growth plate since the growth plate region does not have vessels.

Q5. We have glaucoma (or strabismus) on the eyes. Is that related to Morquio disease or not?

Ans. According to the textbook or common sense among doctors, we could say it is unrelated. However, the recent registry data or the information from the patient may change such concept. As Morquio patients live longer, these eye symptoms may be more popular. Therefore, we need more detail analysis before the definite conclusion of relation between Morquio disease and these eye issues.

Again, there is no statistical analysis made on these subjects. None of doctors and scientists do not know the clear answer. Since we have a schedule to the natural history program in a large scale from many Morquio patients, we may have more precise answer.

Q6. The growth hormone will work on Morquio patient?

Ans. It will be unlikely to have a huge benefit by using the growth hormone since Morquio patients have sufficient growth hormone in the body. The fundamental issue of Morquio disease is caused by destruction of the growth plate with the accumulation of keratan sulfate in the cartilage cells. Therefore, we have to clear such storage material. Some patients have used the growth hormone in the past. However, till now, we have not noticed the huge benefits have occurred. Of course, there is still argument on when or how to treat the patient by the growth hormone since only several patients have used it so far.

Q7. Why is it so difficult to develop of Morquio A drug?

Ans. We have several reasons.

1. It is a very rare disease (1 out of 200,000-300,000 births). Therefore, only 1200 patients are suffering from Morquio A disease in developed countries. Therefore it is not so easy for the big company to have an interest to develop the drug.
2. It is systemic bone disease. It is a challenge to improve the bone lesions compared to other visceral organs like liver, spleen, kidney etc.
3. Enzyme deficient in Morquio patients is not easy to be purified since the enzyme is unstable.

In addition, we have to need the detailed preclinical tests (mouse, monkey, rat etc.) to go forward to the clinical trial.

Q8. How much will enzyme replacement therapy or other treatment like gene therapy work on Morquio patients?

Ans. This is a very critical question but also it is very difficult to answer at this moment. Since we have never treated Morquio patients, we can not predict how much effective. Especially, many factors must be considered: age, clinical severity, the extent of storage material, current clinical situation, condition of the bone deformity etc. The effectiveness will vary by individual patient. Some patients will get more benefits but others will get less benefit. According to the other types of MPS patients treated by enzyme replacement

therapy, to improve bone lesions, it will take time. Early treatment at an early stage will provide a more benefit. We are treating Morquio A mouse model at a different age currently. Gene therapy is still at quite an early stage on Morquio A, therefore, we can not predict any at this moment. We are currently under way of some other new treatments on Morquio mouse models. We hope that we can answer more clearly.

Q9. Morquio patients can get the child? The child is also affected by Morquio?

Ans. Yes. Morquio patients can have own child. However, special consideration must be done for woman Morquio patients since the lung capacity and abdominal capacity are very small. Generally, woman Morquio patients need Cesarean section at the delivery. The child is not affected by Morquio A unless the partner is a carrier or Morquio A patient.

Q10. Why do Morquio patients have hypermobile joint (loose ligament)? And is there any help to put the wrist bands?

Ans. There are two possibilities: one is because of small bones on the hands and wrists. The other possibility is the connective tissue and ligaments surrounding wrists are severely affected. The wrist bands could be helpful to sustain the grip power. The drawing, writing, and the computer typing can help to maintain the function. All are supportive treatment. Indication of surgical procedures remains uncertain and its consequence is not clear since very few patients have received the operation so far.

Q11. We do not know about Morquio disease. How can we get the information?

Ans. First please ask the expert of your country or region and your each individual national MPS Society. International Morquio Organization will also send the educational CD without any charge. Please ask the available language as well since we have several languages for educational CD.

Q12. What kinds of rehabilitation do we have to take? Any recommendation?

Ans. This is very important since the appropriate rehabilitation will maintain your skills and strength as well as physical activity. Generally, we recommend physiotherapy (swimming), diet therapy (refrain from overweight), fine motor skills (computer, any music instrument, drawing, writing), and walking if possible. Ultimately, each individual patient must find the most appropriate one by him or herself since signs and symptoms are different.

We are now summarizing the rehabilitation methods. Hopefully, we can put the methods in next version of educational CD.

Q. 13 How can we relieve the pain?

Ans. There is no universal method to relieve the pain. Also it depends upon how severe, how often, where, worsening or not etc. We are now summarizing the pain killer methods. Once it is done, we will inform it ASAP.

Q. 14 The pregnant woman who has a baby (fetus) affected by Morquio will have a higher tendency of miscarriage or not.

Ans. Since we do not have any such data scientifically, we can not conclude any on this. However, one thing is true that Morquio kids are born with normal height and weight from our registry data (this is scientific: over 350 patients data). Therefore, it is very hard to tell that you are affected by Morquio at birth. Again, Morquio kinds have normal stature at birth!

Overall, the most miscarriage may not be related to Morquio and that it will be just coincidental or by accident.

Of course, we have to learn this issue from Morquio families more statistically: how often does the pregnant woman who has a baby affected Morquio have miscarriage? Such incidence is higher or not compared with normal population.

We hope that we can conclude this issue in the near future through the registry program.

Q. 15. How can we know about Morquio A?

The foundation is now providing Educational CD for Morquio A. It explains the details on Morquio A from the basic to clinical issues. Since it is the slide presentation, it is easy to understand what is Morquio A! It is absolutely free. Please ask the CD by Mary Smith mbs85705@yahoo.com. *Thanks!*

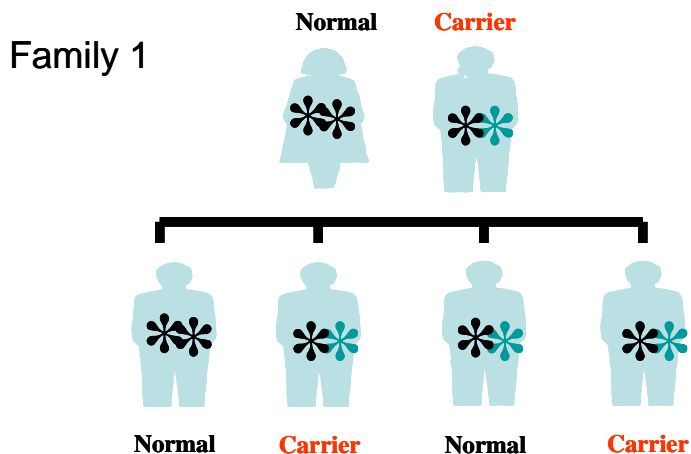
Q. 16. How is Morquio A Disease inherited?

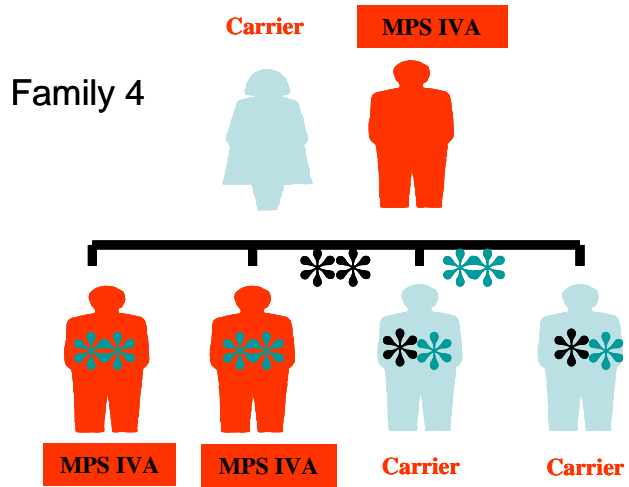
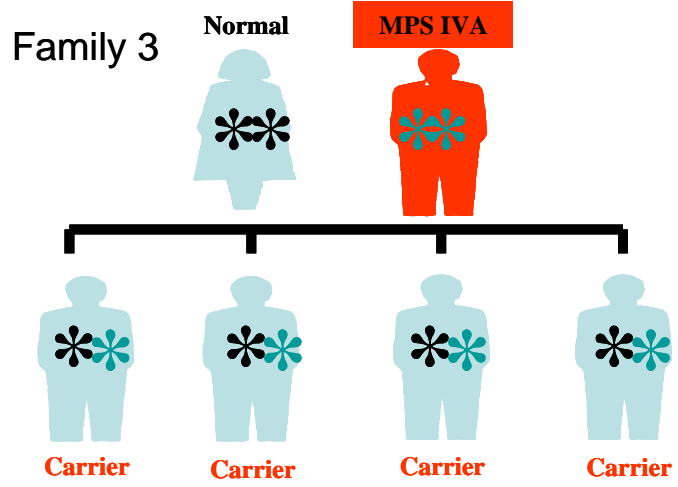
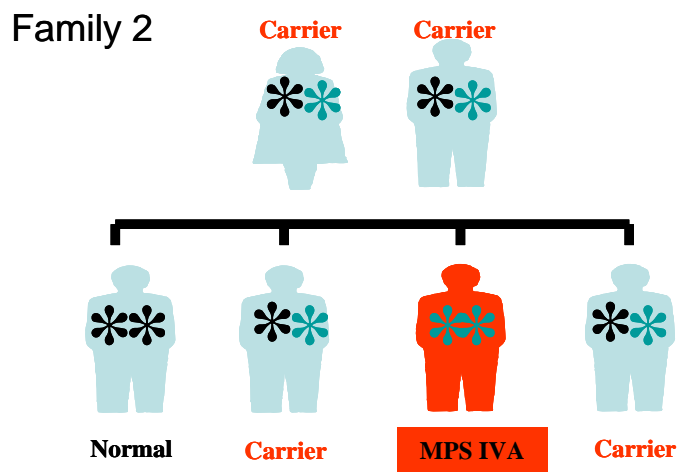
A child with only one parent who is a carrier has a 50% chance becoming a carrier (see Family 1).

If both parents are carriers of MPS IVA disease, with each pregnancy there is a 50% chance the child will inherit one MPS IVA gene from each parent and be a carrier, or a 25% risk of actually having MPS IVA disease. That means, with each pregnancy, carrier parents have a 3 in 4 (75%) chance of having an unaffected child (see Family 2).

If only one parent has MPS IVA and other parent neither has the disease nor is a carrier, all children will inherit the MPS IVA gene from the parent with the disorder and become carriers. None of the children, however, will have the disease (see Family 3).

If one parent has MPS IVA and the other parent is a MPS IVA carrier, there is a 50% chance of having a child who inherits “MPS IVA gene” from each parent and thus has the disease. There is also a 50% chance of having a child who inherits the “MPS IVA gene” from one parent only, and becomes a carrier (see Family 4).





Scientific papers may be difficult to be understood, but if you have any further specific question, please let me know.

Most Sincerely,

President Mary Smith
The Carol Ann Foundation & The International Morquio Organization
8164 W. Circulo De Los Morteros Tuscon, Arizona 85743
Telephone: 520-744-2531 Fax 520-744-2535
<http://www.morquio.com/>
E-mail: mbs85705@yahoo.com

New Address as of Oct 14, 2007

Shunji Tomatsu MD. PhD
Associate Professor
Doisy Research Center Room 307
Department of Pediatrics, Saint Louis University
1100 South Grand Blvd., St. Louis, MO 63104.
Phone number: 314-977-9292
Fax: 314-977-9105
E-mail: tomatsus@slu.edu

Adriana M Montano, Ph.D.
Assistant Professor
Doisy Research Center Room 311
Department of Pediatrics, Saint Louis University
1100 South Grand Blvd., St. Louis, MO 63104
Tel: 314-977-9103
Fax: 314-977-9105
E-mail: montana@slu.edu

Lab phone number: 314-977-9343 or 9104



Educational CD for Morquio (Japanese version)

We have educational CD for Morquio. If you want to know Morquio disease, it will be good educational slides. It explains all issues on Morquio! Please ask The Carol Ann Foundation & International Morquio Organization for this CD. It is completely free of charge! We have this CD for several languages including English, Arabic, Japanese, German, Polish, Spanish etc.

Morquio Project has been supported by grants from the following non-profit organizations (alphabetically):

1. Ariana's Cure Fund for Morquio
2. Austrian MPS Society
3. Austrian Research Society for Mucopolysaccharidoses and Related Diseases
4. Bennett Foundation
5. Care For Carly Foundation
6. Care For Sota Morquio Foundation
7. German MPS Society
8. International Morquio Organization (Carol Ann Foundation)
9. Italian MPS Society
10. Jacob Randall Foundation
11. Muconetwork
12. National MPS Society
13. Spanish MPS Society

Thanks for all supports and appreciation on Morquio Project.

We also thank for cooperation to join the International Morquio Registry Program for each individual Morquio Family and each national MPS Society.



**We are expanding the activity! Please support our activity!
Morquio Dream Team July 17, 2007**

**Please kindly look at the following web sites to know the variety of activity for
Morquio.**

Address for Morquio Foundations:

The Carol Ann Foundation & International Morquio Organization

President Mary Smith

The International Morquio Organization

8164 W. Circulo De Los Morteros Tuscon, Arizona 85743

Telephone: 520-744-2531 Fax 520-744-2535

<http://www.morquio.com/>

E-mail: mbs85705@yahoo.com

The Bennett Foundation

President Steve Waters

714 Richmond Street

Brunswick, Georgia 31520

(912) 222-1363 or (912) 262-9525
<http://www.thebennettfoundation.org/>
E-mail: swaters@glynn.k12.ga.us

Jacob Randall Foundation for Morquio

President Renee Little
12125 Lexington Park Dr. #208
Tampa, FL 33626
Telephone: 813- 731-8274
Website: www.jacobrandallfoundation.com
E-Mail: rjl197@verizon.net

Ariana's Cure Fund for Morquio

President George Kallas
San Francisco CA
Tel: 650-591-1881
Website: www.arianascure.com
E-Mail: Arianascure@aol.com

Danette Baker Website for Morquio Group

Website: health.groups.yahoo.com/group/Morquio
<http://www.geocities.com/hotsprings/villa/9405>
E-Mail: Morquio@yahogroups.com

Annabelle Bozarth Website

Stephanie Bozarth
Website: <http://www.morquio.org>, www.caringbridge.org/visit/belle Go to Journal
E-Mail: stephbozarth@yahoo.com

Sarah Van Orden Website

Ruthann Van Orden
Website: www.caringbridge.org/visit/sarahvanorden
E-Mail: r_vanorden@yahoo.com

Care For Carly Foundation

Carol Ruhnke
Website: www.careforcarly.com
E-mail: info@careforcarly.com

Annie and Mandy Bellassai Website

Maurizio Bellassai and Betsy Bellassai
Website : www.bellassai.com/morquio
E-mail: Maurizio@bellassai.com

A MIRACLE FOR EDDIE

JENNIFER KIMMINAU

WEBSITE: WWW.CARINGBRIDGE.ORG/VISIT/EDDIEK

E-MAIL: BRADJENI@YAHOO.COM

Isabella Burton web site

Rachel Burton

Website: www.caringbridge.com/visit/bella04

E-mail: ergburton1@yahoo.com

Care for Sota Morquio Foundation

Sota Isomoto Website (Japanese)

Saori Isomoto

Website: <http://www1.ocn.ne.jp/~morquio/index2.html>

E-mail: saori-fanfan.i@docomo.ne.jp

Please let me know if you have any own Morquio web site!