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The Gathered View

PWSA U.S.A.

National Newsletter of the Prader-Willi Syndrome Association (USA)

Postscript on the 'Obese' Gene and Prader-Willi Syndrome: *More Hope*

An update from Robert D. Nicholls, D.Phil., Associate Professor, Department of Genetics, Case Western Reserve University and Center for Human Genetics, University Hospitals of Cleveland

In the February issue of *The Gathered View*, we discussed the implications that discovery of a mouse "obese," or *ob*, gene had for Prader-Willi syndrome (PWS). While it is clear that there is no direct relationship, the possibility of an indirect relationship of *ob* to PWS is under examination at this time. New research gives hope that there need not be any genetic relationship between PWS and *ob* for there to be therapeutic potential in the *ob* findings.

Since the February article, new research has been published in which the *ob* mice, which are normally significantly hyperphagic [excessive eaters] and obese, were given injections of the *ob* protein over the period of one month. These *ob* mice lost, on average, 40 percent of their body weight due to a decrease in hyperphagic behavior. Thus, the mice were able to restore appetite control towards normal. Interestingly, these same authors reported that normal mice lost about 12 percent of their body weight under the same treatment. This finding suggests that the therapeutic value of the *ob* protein is likely to not be limited to those with *ob* mutation, raising hopes for its use in appetite (and hence weight) control in various human obesity conditions. Importantly, there were no apparent side-effects, at least during the treatment period, but longer-term studies and human trials are necessary.

"... the therapeutic value of the 'ob' protein is likely to not be limited to those with the 'ob' mutation, raising hopes for its use in appetite (and hence weight) control in various human obesity conditions."

Given the unique characteristics of Prader-Willi syndrome, it is quite possible that this population of individuals will be most likely to benefit from treatment. As human trials come to fruition (as now seems likely from the latest research), we have reason for hope.

From Discovery to Hope: 'Ob' Research Milestones

Last fall, Jeffrey M. Friedman of Rockefeller University in New York announced that his research team had discovered a gene in mice that, when it malfunctions, causes obesity. Located on chromosome 6 in mice (and chromosome 7 in humans), the gene normally prompts fat cells to produce a protein that travels to the brain and signals when the body has enough fat stored; the brain responds by reducing appetite or changing metabolism. In mice with a mutation in that gene, the protein is not produced and the brain does not receive the signal to curb food intake. Although other genes also play a role in obesity, the researchers who identified this first obesity-related gene claimed the name "obese gene" (*ob*, for short).

With the success of *ob* protein injections in mice (noted by Dr. Nicholls at left), the prospect of new diet treatments for humans—based on synthetic production of the missing protein—led to a bidding war for the right to work with the *ob* gene in developing a drug. The winner, a biotechnology company named Amgen, located in Thousand Oaks, California, reportedly offered $20 million for initial rights to work with the *ob* gene—the highest amount ever paid for a gene.

Of special interest to PWSA members: Amgen's top researchers have been in contact with Dr. Suzanne Cassidy, chair of PWSA's Scientific Advisory Board, to enlist PWSA's help in understanding the role of the *ob* protein in PWS, if any.

inside

The Prader-Willi Syndrome Association (USA)

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Out of the Office

by Russ Myler, Executive Director

A member called to let us know she and her husband were fighting their state bureaucracy to obtain services (sounds familiar, doesn't it?). I thought this was going to be one of those calls where frustration would rule. Not so! She told me they had gone to their senator to seek help and found out that PWSA (USA) and their chapter had been there first via National Awareness Day. The senator was aware of PWS and the services needed; he helped them get the services started. The mother called to thank the Association for Awareness Day and its results for her.

Awareness Day was a major change in the way national and chapters work together. For the first time the Association provided chapters all the basic materials needed to accomplish a task and coordinated it on a national level. This kind of national support helped make the difference between holding a somewhat successful event and having the highly successful Awareness Day. This shows the potential PWSA (USA) has to benefit chapters and individual members as it develops into a stronger national organization—a future where PWSA (USA) provides the information, tools, and support necessary for chapters and individuals to make a major impact in their area. This is a goal for which I hope we all work.

The Association is growing in every area: demands on phone services for information and assistance have doubled; two new chapters are being formed yearly and need support; existing chapters are adding to their programs and require increased support; the national conference is drawing larger numbers every year, demanding more staff and volunteer time. These increases reflect our success as an organization, but place added demands upon our resources of volunteers and staff and inhibit our growth toward our goals.

Awareness Day was a model for the future, but without the chapter donations from fund raising and major corporate donations this event could not have taken place. The Association is not funded nor the national office staffed to regularly provide that level of service and support to chapters and members. Growing toward our potential is directly linked to increased Association resources.

PWSA (USA) members have proven that they can meet any challenge. We now face the challenge of growing into our potential as a highly effective national, state, and local organization. To accomplish this we must grow our numbers, increase our funding, develop additional leaders, and add to the Association's resources. The ones who will benefit from our future will be those with the syndrome and those who love them. Let's keep going!

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Opinions expressed in *The Gathered View* are those of the authors or editors and do not necessarily reflect the views of the officers and board of directors of PWSA (USA). *The Gathered View* welcomes articles, letters, personal stories and photographs, and news of interest to those concerned with Prader-Willi syndrome.

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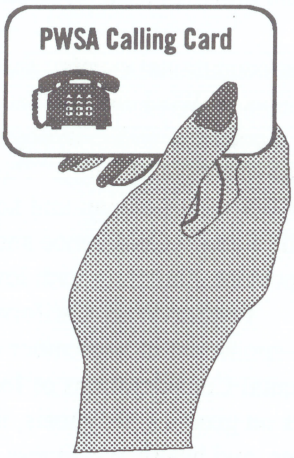
Communications regarding *The Gathered View* or PWSA membership should be directed to the national office of PWSA (USA), 2510 S. Brentwood Boulevard, Suite 220, St. Louis, MO 63144-2326. Telephone 1-800-926-4797 or (314) 962-7644 in the St. Louis area. Fax (314) 962-7869.

This is United Way time for many of you. Please remember that you can designate PWSA (USA) as a recipient of your donation. Some United Way organizations will only give to local organizations, so remember your chapter. Better yet, split your donation between national and chapter.

Calling All Long-Distance Users ...



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(P.S. Don't throw your card away when the calling time is used up. Because of the small run, collectors may be interested.)

COME TO THE 18TH ANNUAL PWSA-USA CONFERENCE JULY 18-20, 1996 IN ST. LOUIS, MISSOURI

As a way to make travel arrangements easier and generate funds for PWSA (USA), we are working with Pat Mann and Regency Travel. **ALL** hotel reservations **must** be made through Pat. We would like to encourage you to use Regency Travel for all your needs to ensure that PWSA will get credit for all reservations booked. Look for more information on registration later, but you can make reservations now by calling:

Pat Mann, Regency Travel, 1-800-784-7581

THANKS TO OUR CONTRIBUTORS

AUGUST 1 THROUGH SEPT. 25

AWARENESS DAY Chapter Fund-sharing

Prader-Willi Association of Michigan
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Dr. Robert Nicholls
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Ruth Sebben
Palmyra Savings and Building Assoc.
In memory of Bea Maier—
PWSA of Connecticut

Local Happenings—Summer and Fall '95

After a busy spring preparing for Awareness Day/Week and then off to the national conference in July, some of our PWSA chapters still found time to have some fun. The **Prader-Willi Syndrome Arizona Association** held a Summer Swim Party in July featuring a lo-cal lunch, and the **Wisconsin** chapter held its annual picnic in August.

Other chapters have been busy planning educational events: the **Prader-Willi Florida Association** prepares for "A Special Weekend" in Tampa in October, featuring Dr. Frank Diamond, Jr., a pediatric endocrinologist speaking on growth hormone treatment and protein-sparing diet, and a "Pass the Gavel" Party for outgoing chapter president Wauneta Lehman and her husband Bob … **PWSA of Georgia** plans a fall "Family Conference and Retreat" featuring speakers on behavior management, parenting with love, medical updates, and education and legal issues … **Prader-Willi California Foundation,** a PWSA-affiliated organization, co-sponsored in September a one-day "Symposium on the Genetic and Developmental Considerations of Individuals with Prader-Willi Syndrome," with speakers on genetics, diagnosis, life sequences, behavior, nutrition, endocrine issues, and health and fitness issues.

Chapter Calendar

1995

Oct. 13–15 **PW Florida Association** "A Special Weekend," Sheraton Inn, Tampa, Fla. Contact: Nettie Secundy, 305-431-1141

Nov. 4 **PWSA of Wisconsin** meeting, Sun Prairie, Wis. Contact: 608-845-9597

Nov. 11 **PWSA of Ohio** fall meeting, Cleveland area. Contact: 216-741-6778

Nov. 17-19 **PWSA of Georgia** Family Conference and Retreat, Warm Springs, Ga. Contact: 404-518-4795

1996

April 26-27 **New England-New York Alliance** Fourth Annual Joint Conference, Albany, N.Y.

New England/NY Alliance Conference Tapes Available

Audiotapes of information sessions at the April 1995 joint chapter conference are available for purchase. Sessions include: "Overview of Prader-Willi Syndrome," by Robert Wharton, M.D., and Karen Levine, Ph.D.; "Aging and the Adult with Prader-Willi Syndrome," by Suzanne Cassidy, M.D.; "Prader-Willi Syndrome Is Not an Excuse!" by Terrance James, Ph.D.; a panel on residential issues; a panel of attorneys on guardianship and choice; stress management; and conference opening remarks. A full set of 10 tapes is $70 plus $7.00 shipping and handling; individual tapes are $12 plus shipping and handling. For order information, contact: Cambridge Transcriptions, 675 Massachusetts Ave., Cambridge MA 02139, telephone (617) 547-5690, or fax (617) 547-0020.

PWSA Chapters and Affiliated Organizations

(chapter president or contact person)

Arizona *(Annette Ruiz, 602-813-7302)*
Arkansas *(Joyce Banks, 501-664-8511)*
California Foundation (affiliated org.) *(James Koerber, 510-676-6591)*
Colorado *(Florence Gunnison, 303-238-1717)*
Connecticut *(June Smith, 203-763-1063)*
Delaware *(Karen Swanson, 302-836-6213)*
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Utah *(Dennis & Glenna Smith, 801-785-3444)*
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***regional chapters**

States Now Forming Chapters

Indiana *(Leo Schertz, 812-988-0281)*
Iowa *(Wanda Askelson, 319-382-4106)*
Louisiana *(Doris Richard, 318-754-7263)*
Nebraska *(Roger Rhoads, 402-333-8400)*
North Dakota *(Curt Aalund, 701-228-5103)*
Oklahoma *(Gretchen Hannefield, 918-582-0441)*

Scientific Day Report—Part II

The following research was reported at this year's Scientific Day in Seattle. (Two other studies were summarized in the last issue of The Gathered View.)

Phenomenology of Obsessive-Compulsive Disorder in Persons with Prader-Willi Syndrome

Research by Elisabeth M. Dykens, Ph.D., and James F. Leckman, M.D., Yale University Child Study Center; and Suzanne B. Cassidy, M.D., Case Western Reserve University and Center for Human Genetics

While food preoccupations are a hallmark of PWS, the disorder features repetitive thoughts and behaviors outside the food arena. Persistent skin-picking is often seen, as are a host of recurrent, intrusive thoughts and behaviors consistent with obsessive-compulsive disorder (OCD). Increased risks of OCD are suggested, and this research evaluated this risk in three ways.

First, the range, scope, and severity of non-food obsessive-compulsive symptoms were identified in 91 subjects with PWS, ages 5 to 47 years. Prominent symptoms included hoarding, ordering and arranging, concerns with symmetry and exactness, rewriting, excessive grooming, and the need to tell, show, or ask. These symptoms were not correlated with maternal obsessive-compulsive features, but were related to increased familial stress.

Second, these symptoms were compared with well-established clinical criteria for OCD. A full 60 percent of the sample met criteria for OCD. An additional 25 percent showed key symptoms of OCD, but did not fully meet diagnostic criteria. Children were just as likely as adults to be classified as having OCD.

Third, symptoms were compared across a subset of 43 adults with PWS, matched on age and sex to 43 non-retarded adults with OCD. The PWS and OCD groups showed comparable levels of symptom severity, including distress and adaptive impairment. Although the PWS and OCD groups had more areas of symptom similarity than difference, the PWS group was more likely to hoard and to need to tell or ask. The OCD group showed more religious obsessions and checking compulsions.

Thus, remarkably high rates of OCD were found in both children and adults with PWS. Although further work is needed, these data suggest a possible gene locus for OCD in the region of chromosome 15 involvement in PWS. These data also have treatment implications in PWS. As OCD likely involves a disturbance in serotonin, persons with PWS may similarly show reduced brain serotonin function. Serotonin reuptake inhibitors are thus likely to be of particular help in reducing these symptoms. Findings also underscore the need for treatment that goes beyond dietary management and that targets relations between family stress and a wide range of compulsive behaviors.

Publications now available from PWSA

Nursing Management

by Geraldine M. DiCosimo, M.S., R.N., C.S.

20-page booklet guides nurses, school health personnel, and other health care practitioners through the essential health issues that arise in the various stages of PWS. $5.00 per copy (includes U.S. shipping and handling; non-U.S. orders will be billed for actual shipping)

Nutrition for Adolescents and Adults with Prader-Willi Syndrome

by Karen H. Borgie, M.A., R.D.

24-page booklet for families and professionals who manage diets of those with PWS; includes worksheets for calculating body mass index and calorie needs. $5.00 per copy (includes U.S. shipping and handling; non-U.S. orders will be billed for actual shipping)

To order, contact PWSA (USA) at 1-800-926-4797, 2510 South Brentwood Blvd., Suite 220, St. Louis, MO 63144-2326.

The Chickenpox Vaccine

Given the tendency in PWS toward skin-picking, chickenpox, with its itchy blisters and scabs, is a disease worth trying to avoid. Fortunately, the Food and Drug Administration this year approved the long-awaited chickenpox vaccine.

Chickenpox—or *varicella*—is a common childhood viral disease that is highly contagious but usually mild and not life-threatening. The most common complication from chickenpox, however, is bacterial infection of the skin. The disease occurs most frequently in children from ages 6 to 10, and the peak times for outbreaks are winter and early spring.

The American Academy of Pediatrics recommends the new vaccine for all children 12 months and older and says it can safely be given with other childhood immunizations. Children older than 13 years who have no history of chickenpox and have never been immunized against the disease should get two doses of the vaccine 4 to 8 weeks apart.

While it's possible for the chickenpox vaccine to cause a rash, it is much milder than a full case of chickenpox.

If a person has not been vaccinated and is exposed to the chickenpox virus, another drug—acyclovir—may be of help. This is an oral medication that can reduce the severity of the disease, if it is administered within the first 24 hours after the rash appears.

For more information, consult your pediatrician.

(Reference: Chickenpox and the New Vaccine—Guidelines for Parents, by the American Academy of Pediatrics)

Growth Hormone and Prader-Willi Syndrome

by Phillip D.K. Lee, M.D.

Dr. Lee is a pediatric endocrinologist who serves on PWSA's Scientific Advisory Board. He is Director of Research and Scientific Affairs for Diagnostic Systems Laboratories, Inc., Webster, Texas; Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, Texas; and Endocrinology Consultant, The Prader-Willi Syndrome Clinic, Texas Children's Hospital, Houston.

One of the most consistent features of Prader-Willi syndrome (PWS) is short stature. The short stature is due to a poor rate of growth during childhood and adolescence. The cause of this poor growth rate is not completely known.

Growth hormone, also known as GH, is one of the major hormones which control body growth. Children who are deficient in GH do not grow normally and, if not treated, end up as short adults.

Recent studies suggest that many children with PWS may have GH deficiency. Furthermore, it appears that children who have PWS and GH deficiency grow much better when they are treated with GH injections. This article summarizes information that is currently available regarding GH and PWS.

Abbreviations used in this article:

PWS means Prader-Willi Syndrome
GH means Growth Hormone
IGF-I means Insulin-Like Growth Factor-I
IGFBP-3 means IGF-Binding Protein-3

What Is GH?

GH is a protein hormone which is produced in an area of the brain called the pituitary gland. GH is released from the pituitary gland into the bloodstream, where it is carried throughout the body. Certain parts of the body are able to take up the GH from the bloodstream. The GH which is taken up by the body is used in many ways.

One of the main effects of GH is to stimulate production of other growth-promoting proteins. GH itself has little or no direct effect on body growth. However, by stimulating production of other growth-promoting proteins, GH has important indirect effects on growth.

One of the most important growth-promoting proteins which is stimulated by GH is called Insulin-Like Growth Factor-I, or IGF-I. IGF-I is produced by the liver and in other parts of the body. IGF-I is then either taken up by neighboring cells or is carried in the bloodstream and taken up by cells in other parts of the body. IGF-I directly stimulates the growth of cells.

In the bloodstream, IGF-I is carried by several bigger proteins, called IGF-binding proteins. The most important of these IGF-binding proteins is called IGFBP-3. In a way, IGFBP-3 acts like a delivery truck for IGF-I.

What Is GH Deficiency?

By definition, GH deficiency means that the body makes abnormally low amounts of GH. When this happens, the blood levels of GH are low and the levels of IGF-I and IGFBP-3 are also low.

Complete GH deficiency (also known as *classical* or *absolute GH deficiency*) occurs when there is something wrong with the pituitary gland itself. For instance, children can be born with all or part of the pituitary gland missing, or the connections between the pituitary gland and other parts of the brain or the bloodstream may be abnormal. The pituitary gland can also be damaged later in life by tumors, trauma, or other events. In all of these cases, the pituitary gland is unable to produce and/or release adequate amounts of GH into the bloodstream. Consequently, growth-promoting proteins which depend on GH, such as IGF-I, are also produced in low amounts. If this occurs during childhood, the body will not grow normally.

There are many other forms of GH deficiency. In some cases, the pituitary gland appears to be normal; however, GH is released in abnormally low amounts. This is sometimes called *partial* or *secretory GH deficiency.* In other cases, GH is produced normally but the body is unable to take up and use the GH which is present in the blood stream. This is called *GH resistance*. In all of these cases, the net result is that the blood levels of the actual growth-promoting proteins (such as IGF-I and IGFBP-3) are low and the body is unable to grow normally.

How Is GH Deficiency Diagnosed?

GH is normally released into the bloodstream in little bursts during the day and a few larger bursts at night. Most of the time, GH levels in the bloodstream are low. Therefore, a typical random blood sample will have a low GH level in both normal and GH-deficient individuals.

There are several tests to measure the maximum amount

of GH which the body can produce. Most of these tests involve taking multiple blood samples over several hours to see the patterns in which GH is released into the bloodstream. For some types of GH tests, medications may be given to stimulate the release of GH into the bloodstream and blood is then sampled every 30 minutes for two to four hours. Another kind of test involves blood sampling every 20 to 60 minutes over an entire 24-hour period without giving medications. Each physician who performs GH testing has his or her own opinions about which tests are necessary.

"... traditional GH testing may not be required to make a diagnosis of GH deficiency but is often required for third-party coverage of GH treatment."

These tests are very reliable for diagnosing complete GH deficiency since the GH levels are always low in all blood samples taken from individuals with this condition. However, these tests do not help to distinguish those individuals who might have partial GH deficiency or GH resistance. GH levels in partial GH deficiency can be very close to or even within the normal range during this type of testing, even if the levels are low during a normal day. GH levels in GH resistance are typically normal or high.

Since GH deficiency of any type almost invariably leads to low levels of both IGF-I and IGFBP-3, measurements of these proteins in the blood may be an alternative way of detecting GH deficiency. In some respects, measurement of IGF-I and/or IGFBP-3 levels may be a more accurate reflection of the effects of GH since it is IGF-I which actually causes the body growth. In addition, unlike GH testing which requires multiple samples and medications, IGF-I and IGFBP-3 levels can be measured in a single blood sample without prior medication.

"An international group of GH experts met recently... and agreed upon recommendations that GH testing methods be updated."

One reason that GH testing has been more commonly used is that accurate laboratory methods for measuring IGF-I and IGFBP-3 have not been available until just a few years ago. On the other hand, laboratory methods for measuring GH have been available for several decades. However, now that IGF-I and IGFBP-3 can be accurately measured, these tests may be preferable to traditional GH testing in selected cases. Another reason is that many third-party insurers require traditional GH testing before they will approve reimbursement for GH treatment. An international group of GH experts met recently in Portland, Oregon, and agreed upon recommendations that GH testing methods be updated. These recommendations may help to reduce the need for traditional GH testing procedures.

What Is Known About GH in PWS?

Because of the short stature and certain other characteristics of PWS, there has been a theory that something might be wrong with GH secretion in PWS. However, for several reasons, studies of GH secretion in PWS have not been very decisive.

First, until very recently, strict criteria for the diagnosis of PWS have not been available. Over the past few years, strict criteria for diagnosis of PWS have been proposed by the PWSA. Furthermore, it is now understood that most, if not all, cases of PWS are associated with defects in chromosome 15. Therefore, it is much easier to be certain that all of the individuals involved in a study have true PWS.

Secondly, traditional GH testing in PWS almost always shows low levels of GH secretion, indicating GH deficiency. The complicating factor is that PWS is also associated with obesity. Obesity itself can lead to low levels of GH secretion. However, obese children who do not have PWS grow normally despite low GH levels. This is not the case in PWS.

"... children with PWS often have abnormal growth and low levels of IGF-I and IGFBP-3. This combination... is strongly suggestive of GH deficiency."

Finally, accurate measurements of IGF-I and IGFBP-3 in PWS have, until recently, not been available. However, it is now known that many children with PWS have extremely low levels of IGF-I and IGFBP-3 in their blood, even when the measurements are corrected for the effects of age and sex. These low levels are particularly apparent after the age of about 5 years. In obese children who do not have PWS, IGF-I and IGFBP-3 levels are usually normal or high.

Therefore, low GH levels are observed in both PWS and obese children without PWS. However, unlike non-PWS obese children, children with PWS often have abnormal growth and low levels of IGF-I and IGFBP-3. This combination of low GH, low IGF-I and IGFBP-3 and short stature is strongly suggestive of GH deficiency.

What About GH Treatment?

At the current time, GH is approved by the FDA only for the treatment of traditional GH deficiency in children: abnormal growth or other suggestive signs and symptoms coupled with low levels of GH measured during traditional GH testing. GH also appears to be effective in the treatment of short stature in other conditions which are not associated with traditional GH deficiency (for example, Turner's syndrome), but full FDA-approval for these uses has not yet been issued. Many insurance companies and other third-party payers will not reimburse medications for non-FDA-approved uses. This is an important point, since GH treatment is very expensive ($10,000–$40,000 per year).

GH treatment involves daily injections which are given at home. The GH dosage is adjusted according to a child's weight and the pattern of the growth response. Therapy should be monitored by an experienced physician at frequent intervals, usually every three or four months. Treatment is usually continued until a child has stopped growing or has reached an adequate height.

Limited data show that children with PWS who have GH deficiency respond very well to GH treatment. In one study of 12 children with PWS (proven by examination and chromosome testing) and low GH, IGF-I and IGFBP-3 levels, all of the children had increased IGF-I and IGFBP-3 levels and all had an increased rate of growth during GH treatment. The rate of height growth typically doubles during treatment. In some cases, more dramatic results are seen. This is very similar to the type of response which is seen in GH-deficient children who do not have PWS. There is no particular reason to expect a different GH response in GH-deficient children with PWS as compared with other GH-deficient children, and no significant differences have been observed.

Does GH Have Other Beneficial Effects?

GH causes an increased growth rate in children by stimulating bone growth. Recent studies show that GH can also lead to an increased amount of muscle tissue, a decreased amount of fat, and a change in the distribution of body fat in both GH-deficient and non-GH-deficient children and adults. It is not known whether these effects are medically significant. For instance, although muscle tissue mass may increase, it is not known whether muscle function and strength also increase significantly. Increased apparent muscle mass has been observed in GH-deficient children with PWS who are treated with GH. However, full muscle function testing has not been done.

"Recent studies show that GH can also lead to an increased amount of muscle tissue, a decreased amount of fat, and a change in the distribution of body fat..."

GH treatment has two main effects on body fat. First, GH treatment causes a relative shift of fat away from the abdominal area and into the hips and limbs. Secondly, GH treatment can cause a decrease in total body fat in individuals who are following a calorie-restricted diet. In other words, GH treatment is unlikely to have a significant effect on body fat if a person is overeating. In our studies of GH-deficient children with PWS, apparent muscle mass and height increased in virtually all cases. However, the total amount of fat decreased only in those children who were following a recommended diet. In other cases, the amount of body fat continued to increase at an excessive rate, although the distribution of the fat did tend to shift from the abdomen to the hips and limbs.

GH is not yet approved by the FDA for treatment of obesity or low muscle mass. Therefore, these effects on fat and muscle should not be the primary basis for deciding on treatment unless the GH is given as part of a specific scientific research study.

What About Side-Effects?

When given to GH-deficient children in usual recommended doses, GH has few major side effects. Transient, usually mild, symptoms of water retention can be observed, but this is more common in adults who receive GH. Studies in Japan several years ago indicated that GH treatment might increase the risk for leukemia. However, ongoing international studies have failed to show any increased risk of leukemia or other cancers in GH-treated children.

GH has a natural effect to counteract insulin (the main hormone in the body which controls blood glucose levels). Because of this, some individuals may develop diabetes mellitus during GH treatment. This is especially the case for individuals who are grossly overweight (more than twice their ideal body weight). This is because obesity itself also counteracts insulin. Diabetes mellitus which is associated with GH treatment goes away if the GH treatment is stopped or if the GH dose is significantly decreased.

Obese children are also predisposed to bone and joint problems, including a hip-joint condition known as slipped-capital femoral epiphysis (SCFE). In addition, children with PWS have an apparently increased risk for back problems such as scoliosis and kyphosis. It is not known whether GH treatment increases the risk for these conditions. Children with PWS should be examined by a physician regularly to detect SCFE, scoliosis, and any other bone and joint problems even if they are not receiving GH treatment.

It should be kept in mind that most of the information about the side effects of GH treatment is based on studies of GH-deficient children who do not have PWS. There are relatively few GH-deficient children with PWS who have received GH treatment for long periods of time. Therefore, it is possible that side effects of GH treatment may occur in GH-deficient children with PWS which are not observed in other populations.

Should My Child Be Considered for GH Evaluation and Treatment?

GH treatment is a major decision which could lead to years of daily injections for your child and financial concerns for you. The only expected benefit is an increased height. In other words, if a child truly has GH deficiency and is not treated with GH, the only proven consequence is that he or she will be a short adult. Of course, very short adults can suffer handicaps which may limit their ability to function independently. However, before embarking on a course of GH evaluation, you need to decide whether GH treatment is an acceptable option for your child if he or she is found to be deficient. If you feel that your

child would not benefit from an increased height, then GH testing may be unnecessary. This is a difficult decision and should involve consultation with your child's physician.

If you have decided that GH treatment would be an acceptable option for your child, the next step is to determine whether your child has GH deficiency. Remember that GH treatment is approved only for the treatment of GH deficiency. It is not approved for the treatment of obesity, low muscle mass, or PWS per se. To determine if your child has GH deficiency, he or she will need careful medical examination and testing. This evaluation is often done by a pediatric endocrinologist since this specialty typically deals with GH-related problems.

> *"The decision about whether your child would benefit from an evaluation for GH deficiency should be carefully made in consultation with your child's physician..."*

As part of the evaluation, the physician may consider the following points:

1. Your child's growth pattern or growth rate (a k a height velocity). Children with GH deficiency typically have an abnormally low rate of growth, and children with PWS typically have a low growth rate by the time they are about 5 years old. The rate of growth can best be determined by careful measurements taken on a calibrated, wall-mounted measuring device at approximately 6-to-12 month intervals (a general pediatrician's office may not have this type of measuring device). These measurements are compared with standard normal growth rate charts.

PWS children with tall parents may be taller than PWS children with short parents. In addition, although children with PWS do not have normal puberty, they can enter puberty early. This may cause them to grow rapidly even though their final adult height is abnormally short. Finally, scoliosis and other back problems can cause a false-low estimate of height. Your physician may need to do special X-rays (bone age X-rays, back X-rays) if these possibilities are noted on examination. A bone age X-ray is also useful to determine whether your child's growth plates are open, in which case they might still respond to GH treatment.

2. Other possible causes of poor growth. This might include tests for thyroid problems and kidney problems. Although these conditions are not more common in PWS, they do occur with significant frequency in the general population. A screening test for diabetes mellitus may also be included.

3. Diet and exercise assessment. As pointed out above, GH treatment is not a good option for children who are not following a recommended diet. Therefore, it is very important to have a good diet and exercise program (with successful weight control) in place before proceeding with GH testing and possible treatment.

4. IGF-I and/or IGFBP-3 levels. If these levels are abnormally low and there are other signs of GH deficiency, your physician may then recommend GH testing. The specific details of the testing will depend on the type of test that is recommended. As discussed above, traditional GH testing may not be required to make a diagnosis of GH deficiency but is often required for third-party coverage of GH treatment.

After completing this assessment, the physician will make a recommendation regarding GH treatment. If treatment is recommended, you will need to learn how to administer the daily injections. In addition, your child will need to return for regular clinic visits, usually at about 3-to-4-month intervals. In the Prader-Willi Clinic at Texas Children's Hospital, the following tests are monitored at each visit for each child who is on GH treatment: height, weight, body fat, lean mass, and physical examination. Body fat and lean mass are determined using special instruments similar to an X-ray machine. The GH dose is adjusted according to the weight and growth pattern. Bone density studies are also done at 1-to-2-year intervals, and lab tests may be done if symptoms of diabetes mellitus or other complications appear.

In addition to this traditional approach to GH evaluation and treatment, there are a few centers that are conducting research into the effects of GH treatment on muscle, fat, and other measures in children and adults with PWS. Your local university medical school or hospital pediatrics department and the Scientific Advisory Board of the PWSA may be able to provide more information about such studies.

Summary

In summary, recent studies indicate that PWS is associated with an increased occurrence of GH deficiency. For children with PWS who have typical signs, symptoms, and laboratory tests that confirm GH deficiency, GH treatment may be effective in improving the rate of growth. Although GH has other effects, some of which might be beneficial in PWS, these effects cannot be used as the primary basis for GH treatment except as part of a research investigation. In addition, children with PWS and GH deficiency must be carefully monitored for side effects, complicating factors, and treatment effectiveness. The decision about whether your child would benefit from an evaluation for GH deficiency should be carefully made in consultation with your child's physician and should be based on the overall decision regarding the acceptability of GH treatment as an option for your child. □

SUGGESTED READING

Management of Prader-Willi Syndrome, second edition. Edited by L.R. Greenswag and R.C. Alexander. Published by Springer-Verlag, New York, for the Prader-Willi Syndrome Association, 1995. Chapter 3. "Endocrine and metabolic aspects of Prader-Willi syndrome" (pages 32-60). Written by Dr. Phillip D.K. Lee.

"Diagnostic controversy: The diagnosis of childhood growth hormone deficiency revisited." *Journal of Clinical Endocrinology and Metabolism*, Vol. 80, No. 5, pages 1532-1540, 1995. Written by Dr. Ron G. Rosenfeld and 15 other international GH experts.

Success with Community-Based Employment

by Norma Vogel of Charles River Industries, Needham, Massachusetts

A recent issue of *The Gathered View* addressed the issue of vocational planning and job placement for people with Prader-Willi syndrome. Currently, the need and desire for community-based employment and the phasing out of sheltered workshops have raised questions and changed preferences among those with PWS and their families.

Charles River ARC, in Needham, Massachusetts, through its day services, Charles River Industries (CRI), is proving that individuals with PWS can be successful within community-supported employment.

Charles River Industries has provided vocational training and job-placement services for over three decades. CRI has served individuals with PWS for many years, in both our supported employment and facility-based programs. One individual with PWS worked successfully in a lamp shade manufacturing plant. Another consumer worked as a veterinary assistant. Both were on the company payroll and received training, support, and ongoing supervision from CRI staff.

In July 1995, CRI was awarded a five-year contract from the Massachusetts Department of Mental Retardation (DMR) to develop and maintain supported employment opportunities for five persons with PWS. DMR sought these specialized services because the individuals were clearly being underserved by existing sheltered work programs. Our new program, called "Work Concepts," now serves seven adults with Prader-Willi syndrome, each with an objective to work within the community.

CRI staff within Work Concepts are specially trained regarding PWS, supported employment, and behavior management. The staff-to-consumer ratio is very strong (one vocational supervisor to two consumers) for individualized attention and intensive supervision. In addition to the vocational supervisor, an employment specialist provides case management, does vocational and behavioral assessments, coordinates therapeutic support services, and works closely with consumers' families and residential staff. The CRI job developer seeks out the optimum job match based on each person's preferences, skills, and support needs.

While the vocational assessment process is ongoing, with many different avenues to explore, the job development process also has many issues to carefully consider: identifying which consumers work well together and have similar job interests (a ratio of one staff to two consumers means two individuals will work at the same job site together); finding employment with limited access to food sources, and investigating if food is an integral part of the company culture; determining how break time and bathroom visits will be supervised; and many other issues that may seem minor or insignificant for other individuals to whom CRI provides supported employment services. However, for workers with PWS, these issues can have a major impact on their success within community employment, in addition to the more general issues of good matching of skills and interests.

We are delighted to report that since the start of Work Concepts in July, two program participants found employment and are successfully working, processing merchandise and clothing for a well-known retail department store. At the time this article was drafted (mid-September), they had been working for well over a month and had received only accolades from their employers!

Most of the consumers in the Work Concepts Program have taken an active role in their job search, and we know it will not be long before the other individuals with PWS are successfully working within the community as well.

For more information about Charles River Industries or our Work Concepts Program, write or call our Director of Job Development and Marketing or the Director of Supported Employment at (617) 444-4347, Charles River Industries, 989 Central Avenue, Needham, MA 02192.□

To the Home Front *from the editors ...*

We thoroughly enjoy publishing stories about the successes and accomplishments of our children and adults with PWS. Such accounts are a source of both pride and hope. But we also know that there are many, many parents whose children are not doing so well, and perhaps neither are they. Reading about how well others are doing may make some feel even more alone as they try to cope with the syndrome. We encourage those parents, too, to share with us their struggles, heartaches, problems, and distress. There may be multiples of "someone out there" who need to read about just that—that they are not the only ones who are having a hard time. PWSA and *The Gathered View* are here not only to provide information, but to offer support to each other in our extended family of PWS. Perhaps you are the one whose letter will do just that for another parent.

Lori Newell, age 24 and one of Charles River Industries' program participants, is the author of the poem below. At age 5, she was diagnosed with a brain tumor. After cancer treatments in her early teens, she developed the characteristics of Prader-Willi syndrome. Lori's condition has been called "Prader-Willi like syndrome" or "acquired" Prader-Willi syndrome. Today Lori is working successfully at a well-known retail store where she processes garments in the stockroom. When she's not working, Lori expresses her creative side in writing, music, and crocheting.

Prader-Willi Syndrome

by Lori Newell

I have Prader-Willi like Syndrome,
I am aware of this, I know,
and because I am aware of this,
I am able to grow.

I have a problem as you can see,
This problem involves food.
Please don't offer me any, of any kind,
I am being polite, not rude.

Some things are harder for me to learn,
Though I am easy to teach.
If you show me hand over hand, you'll know,
that it's my heart you've reached.

Sometimes I might perseverate,
or say things over again.
Please be patient with me, and I will know
that you want to be my friend.

You don't have to hate me, for I am the same,
although I have problems too.
And maybe someday when the sky touches ground,
My one great wish will come true.

My wish is that I could be the same
as you, or him, or her,
and that this disease would disappear,
be gone, finished, no more.

But until this day does come for me,
I still must carry on.
I still must live the same life I've lived
with all the rights and wrongs.

It's time for me to say "so long,"
but thank-you for hearing me out.
I told you before, but I'll say it again,
this is what my life is about.

Being a Dad

by Brian Norton,
Wentzville, Missouri

Bowhunting is one of my favorite things to do in the fall of the year. So you can imagine how happy I was to finally be in the woods. Funny thing was, I didn't even care if I saw a deer that day. Because I couldn't seem to stop myself from crying. Here I am six foot three, two hundred pounds of sobbing flesh. I had a very good reason. It was a reason some of you reading this article know all about. My son Andrew was just diagnosed with Prader-Willi syndrome. And this seemed like a perfect place to feel sorry for myself. No one around for miles to hear or see me crying my eyes out.

That was four years ago. And today when I remember that day, I feel a little foolish. Not because I was sad, but because now I see all of the things my son has accomplished for himself.

Andrew has never met a stranger he didn't like. People who have met him tell me how cute he is. Like I didn't know?

Andrew can walk, talk, run, ride a tricycle, climb stairs, and swing on a swingset. Pet the meanest dog in the county! Fight with his brother and sister! And every once in a while say a few cuss words!

And now as I sit here, I can remember each one of his accomplishments as it happened. Because, you know, these kids are a little slower than other kids. Each time Andrew did one of these things, it made me think about the first day I found out he had Prader-Willi, and how silly I was to be anything but proud of my son!

Editor's note: Brian Norton, who often writes about his son Andrew, age 4, in the Missouri View newsletter, was a natural to be the first father to contribute to our new "Being a Dad" feature. We thank Brian and encourage other dads to write, long or short, about what it is like for them to be the dad of a child with Prader-Willi syndrome. Too often the feelings and experiences of fathers get missed. This is an opportunity to share and perhaps help others better understand and cope.

Ask the Parents

A parent is in need of an alarm device that can be attached to a young child who has a tendency to wander. Any parent who has successfully used such a device or knows of a source is asked to call the national PWSA office—1-800-926-4797.

Tips for Reducing Stress ... and Surviving the Holidays

by Gail Overton, M.S., L.N., PWS Project Training Coordinator, State of New Mexico, and member of the PWSA (USA) board of directors (adapted from the PWS Project News)

The holiday season is once again upon us, and that conjures up visions of traditional family celebrations. But we may also be visited by visions of impending tantrums, missing foods, defiance over medication regimens, and high blood sugars.

There is hope for avoiding the possible anxiety and stress of the holiday season. The key is to be prepared and set definite boundaries. Here are some strategies that may help in keeping the season safe and sane.

1. Visualize It First

An excellent way to prevent problems is to anticipate possible problems by playing a mind game called "what if." Mentally visualize all kinds of situations, see the possible traps, and find the solutions. Some situations may be centered on serving small portions of favorite foods, having appropriate goodies accessible and within reach, suggesting a long walk after the holiday meal, and testing blood sugars in a timely manner even when other activities are happening. The list of "what if" situations can be lengthy, but forethought could save the day.

2. Fine-tune Your Communication Skills

- Listen to the other person and hear the "intentions" behind their words.
- Acknowledge and reflect on what the other person has said so you both understand the message and are on the same wavelength.
- Be positive and firm in your manner when stating your own remarks.
- Begin sentences with "I like" or "I need," which let others know you are expressing your own feelings. Others are more likely to respond to you positively, and confrontations may be avoided.
- Be sure all boundaries are understood. Speak often of which behaviors are acceptable and which are not.
- Don't change the rules in the middle of the game—this can cause confusion. Solicit input from those who need help by asking what boundaries they are willing and able to set for themselves, and which ones they are willing to let you set for them.

Toy Shopping?

Want toys with developmental as well as entertainment value? Here are three sources of help you might consider in planning a special purchase for a child with Prader-Willi syndrome:

Toy Guide for Differently Abled KIDS!—Toys "R" Us has issued a new edition of its coded guide to toys that have specific play benefits for children with special needs. The catalog is endorsed by the National Parent Network on Disabilities, and the toys were tested by Lekotek, the national organization that operates "play libraries" nationwide. If you can't get a copy at your local Toys "R" Us, write or call NPND, 1600 Prince St., #115, Alexandria, VA 22314, (703) 684-6763.

Lekotek Toy Resource Helpline—1-800-366-PLAY—You can call this toll-free number to discuss your individual child's abilities with trained Lekotek Leaders, who are experts on toys, play materials, and creative play ideas for children with disabilities.

The Dragonfly Toy Company—1-800-308-2208—offers a catalog of less common toys for children with disabilities (selected from other catalogs and around the world), a play therapist on staff to advise buyers, and toy search and "wish list" services. Call to enroll your child in their free "club," or browse their catalog via computer on the World Wide Web (search for "Dragonfly").

3. Save Calories

By cutting down on the average prescribed daily intake the whole week before the holidays, you can save calories so that the holiday meal can be larger, including a little dessert. By omitting a fruit and a bread serving each day for seven days, you can save 840 calories. An extra 840 calories can go a long way and not affect the overall weight of the person with PWS if you allow special treats and larger meals only on the actual days you hold celebrations.

Other tips:

- Don't look at the holidays as a "season." That sets you up for weeks of partying and the constant presence of food.
- Use low-calorie vegetables as fillers and appetizers before or with meals to fill up on and prevent overeating.
- Freeze or give away foods that are left over from your holiday dinners.
- Don't forget to increase exercise during the holidays. This can help burn calories and keep blood sugars in check.
- And, last, but not least, experiment with healthier, reduced-fat versons of your favorite recipes. □

Prader-Willi syndrome (PWS) is a birth defect first identified in 1956 by Swiss doctors A. Prader, H. Willi, and A. Labhart. There are no known reasons for the genetic accident that causes this lifelong condition which affects appetite, growth, metabolism, cognitive functioning, and behavior. The Prader-Willi Syndrome Association (USA) was organized in 1975 to provide a resource for education and information about PWS and support for families and caregivers. PWSA (USA) is supported solely by memberships and tax-deductible contributions.

PWSA USA