

Acromegaly Support

Volume 1, Fall 2002

WELCOME

This newsletter and subsequent issues will provide information on different aspects of Acromegaly, from history to diagnosis, and describe innovative treatment options to the most current research studies. Acromegaly is a rare medical condition resulting from an excess production of growth hormone by the pituitary gland. The prevalence of this disease in the United States is about 50 cases/million with over 1,000 new cases diagnosed annually. As a result of its relatively infrequent occurrence, many patients with Acromegaly feel isolated, confused and may become depressed and anxious.

Recognizing that it is only through knowledge that patients are empowered to understand, manage and cope with this condition, we have initiated an Acromegaly support program with the generous support of Novartis Pharmaceutical Corporation.

This endeavor, although originating in three centers, Los Angeles, New York and Boston will eventually become a comprehensive national program.

Support for patients with Acromegaly will be provided at several levels, including newsletters, a website, www.acromegalysupport.org, support group meetings and educational patient conferences. We aim to provide general information on a variety of topics, update you on current research projects, and act as a resource for your medical and social needs.

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In order to provide psycho/social support, patient group meetings will be facilitated by skilled and experienced psychiatrists, social workers and other health care professionals. We will be looking to you, the patient, for feedback to help refine and improve this program. This initiative is exclusively patient-oriented and we look forward to your ideas on how to better serve you.

MISSION STATEMENT

We are committed to providing a reliable and authoritative comprehensive support network for people living with Acromegaly and their friends and family. Compassion, empathy, knowledge, experience and research is fundamental for treating all patients with dignity and respect. Our aim is to educate patients about their disease and empower them through knowledge and support.

We are interested in hearing from patients with Acromegaly. How were you diagnosed? What are your symptoms and how long were they present before your diagnosis? Tell us your story! Please email our Medical Education Coordinator, Rosa Lopez, at lopezrc@cshs.org or write to us at 8631 W. Third Street, Suite 121E Los Angeles, CA 90048. Please, also send us any inquiries or concerns you may have, which we will answer in our Q & A column. This is an exciting venture and we all look forward to helping you help yourself.

QUESTIONS & ANSWERS

Q: What is Acromegaly?

A: Acromegaly is a rare medical condition resulting from excess production of growth hormone from the anterior pituitary gland. In **children and adolescents**, this leads to a marked increase in height, which is due to the effect of growth hormone on bone before the growing ends of the long bones have closed. This superfluous body development results in a condition called Gigantism.

In **adults**, excess growth hormone, and its target hormone IGF-1, produced mainly in the liver, act on bone, as well as other soft tissues and organs in the body resulting in general enlargement of body parts as well as metabolic changes, without an increase in height. In adults, the condition is referred to as Acromegaly. There is usually an associated tumor (swelling) of the anterior pituitary gland in both Gigantism and Acromegaly.

In summary, the underlying cause for both Acromegaly and Gigantism is the excessive amount of growth hormone produced by a benign pituitary tumor. The effect on the body depends on the age of onset in each individual patient.

Q: What are the signs of Acromegaly?

A: In **children and adolescents**, the main feature of excess growth hormone, before the growing ends of the bones have fused, is an increase in height.

In **adults**, there are several signs of excess growth hormone, not all of which are present in every patient:

- Enlargement of soft tissues at the extremities of the body
- (acral)- nose, lips, ears, hands and feet.
- Other areas of soft tissue and organ enlargement include
- the tongue, heart, thyroid gland and internal organs.
- There is an increased incidence of polyps of the large
- bowel.
- Bony and cartilage enlargement includes that of the
- forehead (bossing), lower jaw (prognathism), fingers,
- hands, toes, feet and widening of the long bones. These
- changes may cause joint problems (including arthritis),
- tooth problems, numbness of the extremities and carpal
- tunnel syndrome.
- Skin changes include cosmetic changes, increased
- sweating, acne, greasy skin and skin tags. These signs of
- Acromegaly appear very gradually and typically remain
- unrecognized for several years. Reference to old
- photographs will sometimes help pinpoint the year the
- changes began.

Q: What are the symptoms of Acromegaly?

A: These are varied depending on the size of the pituitary tumor and the duration of excess growth hormone secretion prior to diagnosis and treatment.

Symptoms related directly to the local effect of the pituitary tumor include visual impairment (often initially of the lateral fields of vision), headaches, and rarely compression of nerves supplying the head and neck. Features related to excess growth hormone include sweating, greasy skin, elevated blood pressure, fatigue, sleep apnea, voice changes (deeper), impaired glucose metabolism, diabetes mellitus, elevated blood fat levels, diminished libido, impotence, menstrual irregularities, depression, apathy and social isolation.

NEW MEDICAL THERAPIES FOR ACROMEGALY CONTROL OF GH SECRETION

Normal control of GH secretion from the pituitary gland is under the control of two hormones from a higher center in the brain, the hypothalamus. One of the hormones, growth hormone releasing hormone (GHRH), stimulates GH secretion and the other hormone, somatostatin (SRIF), inhibits GH secretion. After GH is secreted from the pituitary gland, it enters the blood circulation and subsequently binds to specific receptors on the surface of liver cells. The binding of GH to these receptors results in the synthesis of the hormone insulin-like growth factor-1 (IGF). IGF-1 performs several of the actions of GH.

Somatostatin acts, not only in the pituitary gland, but also in several different organs in the body, to inhibit function and secretion. There are five different cell surface somatostatin receptors in the body, each of which has a slightly different structure. The five different somatostatin receptor subtypes are present in different amounts in various organs of the body.

Somatostatin analogues have been the cornerstone of medical therapy for Acromegaly over the past decade. These analogues are modified forms of the natural somatostatin molecule, which have a more prolonged effect in inhibiting GH secretion from the pituitary than the original molecule. Several innovative therapies are currently in various stages of clinical development for Acromegaly.

The first somatostatin analogue, octreotide, in use for the past 15 years, is self-administered 3-4 times daily by subcutaneous injection. A new, long-acting, FDA approved preparation, Sandostatin LAR Depot, is administered by injection into the muscle once a month. Lanreotide Autogel, currently undergoing clinical trials in the USA is a preparation administered by injection under the skin once a month. Somatostatin analogues normalize serum IGF-1 levels in approximately 60% of patients with Acromegaly. Approximately, 10-15% of patients are resistant to these analogues because their tumors lack somatostatin receptors.

Novel preparations that bind more strongly to the somatostatin receptor subtype, which is found in abundance in the pituitary, would inhibit pituitary GH secretion more effectively than somatostatin itself. Analogues that act in this manner are being developed and evaluated in the laboratory.

Another experimental agent, the GH receptor antagonist, Pegvisomant, blocks GH action in the liver. IGF-1 secretion is, thus subsequently inhibited. Normalization of IGF-1 levels occur in more than 90% of patients so far treated. This mechanism of action, blocking the binding and action of GH in all tissues in the body with GH receptors is in contradistinction to the other medical therapies available for the management of Acromegaly, which act at the level of the pituitary growth hormone secreting cells, inhibiting GH production and secretion.

Thus, several new therapies are available and several more are in development for medical management of Acromegaly. The long acting preparations have made drug administration much

easier for patients. Medications that control the adverse effects of excessive GH via different mechanisms of action are being developed. These will broaden the therapeutic options for Acromegaly.

PITUITARY HORMONES

The pituitary is the master endocrine gland responsible for regulating many body functions and maintaining homeostasis. The pituitary is a small bean-shaped gland at the base of the skull, weighing between 0.5 and 1.0 grams. In women, the pituitary gland is larger than in men and increases in size during pregnancy and lactation. The pituitary is composed of an anterior and posterior portion. In the case of the anterior pituitary, hormones are synthesized and secreted from the different cells composing this part of the gland. There are six hormones produced by the anterior gland.

They are:

Growth hormone (GH) regulates growth and also plays a role in the body's metabolism.

Luteinizing hormone (LH) and Follicle-stimulating hormones (FSH) control hormone production from the ovaries and testes and regulate fertility through ovulation (ovaries) and sperm production (testes).

Thyroid-stimulating hormone (TSH) controls thyroid hormone production from the thyroid gland.

Adrenocorticotropic hormone (ACTH) regulates adrenal gland cortisol secretion, which is important for the body's response to stress.

Prolactin (PRL) is necessary for lactation in breast feeding mothers.

The two hormones of the posterior pituitary are synthesized in a higher brain area, the hypothalamus, and then transported in nerves to await secretion from the posterior pituitary. **Antidiuretic hormone (ADH)** and **Oxytocin**

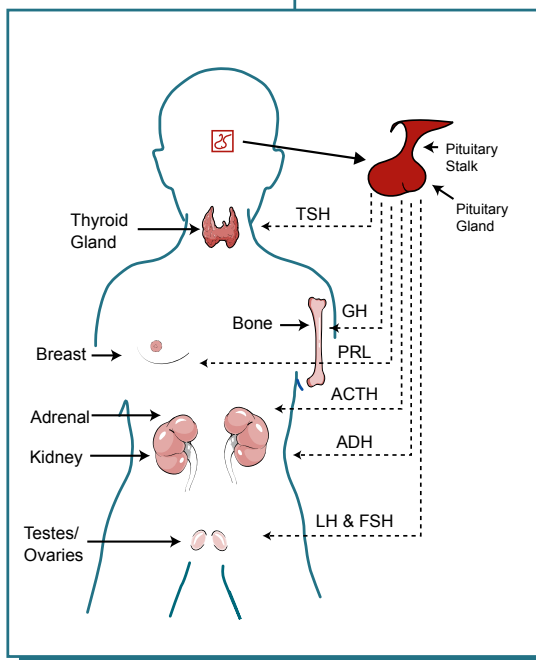
ADH is necessary for water conservation by the kidney, and Oxytocin controls uterine contraction during labor.

management of growth hormone secreting pituitary tumors (Hrayr Shahinian, MD) together with an intraoperative video demonstrating a fiberoptic endoscopic approach to tumor resection. The speakers were then available in break out sessions to discuss research, quality of life issues and answer individual patient questions and concerns.

Feedback from the conference attendees was very positive. All felt that their level of knowledge was increased, and many felt that the experience of meeting others with the same condition was positive, reassuring and comforting. In summary, it was an enjoyable and successful day enjoyed by both patients and faculty. More such events are planned for the future. We will keep you updated and well informed of all events through our website and mail correspondence.

LOCAL NEWS LOS ANGELES

Pituitary Patient Support Group Series - On August 7, 2002, we held our first pituitary support group meeting. This was a highly successful meeting thanks to the active participation of patients, family members and Pituitary Center staff. Dr. Philip Barnett discussed normal pituitary function, which was followed by a group participation discussion/counseling session facilitated by Dr. Margy Sperry. All attendees enjoyed the evening and found it most beneficial in gaining knowledge of their medical condition and feeling a sense of inclusion through management strategies discussed by Dr. Speery. Subsequent meetings too have been well received. These sessions have featured Dr. Vivien Bonert and Dr. Shlomo Melmed discussing pituitary functions, treatment and research.



We plan to continue these meetings every 6-8 weeks. The meetings will consist of short didactic lectures presented by various physicians, followed by a group participation "support" session.

Topics to be covered in upcoming lectures include: Osteoporosis, insurance issues, maxillo-facial surgery, dental health, eye care, gastrointestinal problems, cardiac changes, pituitary radiological imaging, hormone replacement, subfertility, pituitary diseases, medical treatment options, surgical treatment, radiography treatment, hypertension, diabetes, steroids and current pituitary research.

The direction and topics of the support group sessions are open and determined by the participants and facilitated by Dr. Sperry.

Dates, times and locations will be mailed to patients as well as being posted on our website. We look forward to your involvement and support!

Cedars-Sinai Pituitary Center Launches Acromegaly Support Program

May 5, 2002

"LIVING WITH ACROMEGALY"

Fairmont Hotel, Santa Monica, CA

This patient conference was very well attended by patients with Acromegaly as well as their families, significant others and caregivers. The format consisted of a series of didactic lectures followed by breakout sessions. The talks ranged from a historical perspective of Acromegaly (Shlomo Melmed, MD), through discussion of the signs, symptoms and diagnosis of Acromegaly (Philip Barnett, MD, Ph.D), medical management of Acromegaly, including novel therapies in clinical trials (Vivien Herman-Bonert, MD) and quality of life/psychosocial aspects (Margy Sperry, Psy. D, M.F.T.). After lunch, there was a presentation on the surgical

We are endocrinologists specializing in pituitary disease, specifically Acromegaly. As a group, we have extensive experience and expertise in the management of patients with Acromegaly and are involved in related research. Recognizing that patients needs, including updated information, psychological support, and awareness of treatment options are not always adequately addressed in the clinic setting, and through common interests, we have joined forces to establish this support network. Each center will present programs and meetings locally. These will be advertised on the website and in our newsletter.

Visit our website: www.acromegalysupport.org

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Disclaimer:

The information contained in this newsletter is for educational purposes only. It is not intended to be used to diagnose or to recommend treatment for Acromegaly. A physician consult should be obtained to address any medical concerns and to obtain medical treatment.

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