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Southern California Region II
Governor's Newsletter

September 2008 George Sarka, MD, MPH, FACP, FACR, Governor

Governor's Message

Summer 2008 is almost gone and many new items need to be discussed. I would first like to start with your representatives on the Governor's Council. It consists of a diverse group of individuals from throughout the region to represent and discuss the needs of its members. Not only do we have former Governors, practicing internists and university physicians, but now we have a chief resident in Internal Medicine from UCI this year-**Nitanth R. Vangala, MD**. Here is the complete list:

Alpesh N. Amin, MD, MBA, FACP
Thomas C. Cesario, MD, MACP
Philip M. Gold, MD, MACP
Douglas R. Hegstad, MD, FACP
Lawrence K. Loo, MD, FACP
Maher A. Roman, MD, MBA, FACP
Melvyn L. Sterling, MD, FACP, FAAHPM
Jeremiah G. Tilles, MD, MACP
George Sarka, MD, MPH, FACP, FACR
Debra L. Stottlemyer, MD, MBA
Conny Tirtaman-Sie, MD, FACP
Leah Tudtud-Hans, MD, FACP, FAHA, FESC
Nitanth R. Vangala, MD

Region II had it first Educational Dinner Meeting on 8/28/08 in Santa Ana. Two lectures were given that night.. The first was on "*Why Fellowship in the ACP?*" by your governor. This was followed by an excellent and informative speech on "**Complicated Skin Infections: Epidemiology and Management in the Current Era of Resistance**" by **Arthur Jeng MD** of Infectious Diseases at UCLA. Region II hopes to hold many more meetings of this type in different areas of the chapter. Our next Educational Dinner Meeting will be in the Riverside/San Bernardino area on Fabry Disease/Genetics in Medicine in October 2008. As soon as I have the registration information and date, I will pass it on to all members. Remember, these meetings are limited to 35 to 50 members. So register early. I look forward to meeting you at these meetings.

Time is closing in on our Annual Regional Meeting for Southern California for Regions I, II and III which will be held on October 18 and 19, 2008 in Indian Wells, California with a SEP Review Course on October 17, 2008. Registration is free for Medical Students and Associate Resident Members. ACP physicians are $125.00 and Affiliate Members are $150.00. For ACP Members, the SEP Session Fee is $50.00. There are a number of physicians from Region II who will be speaking this symposium as well as a Medical Jeopardy round between medical residents from different medical schools and then between the winning medical resident team and the "*Seasoned Physicians*." Please register early. For the registration form, go to www.acponline.org and click your mouse on meetings for October 2008 and Southern California. I hope to see many of you there. This is a great way to keep up on current events, medical information and socializing with your medical colleagues.

In the winter of 2009, Region II will be sponsoring a CME-symposium on "*Adventures in the History of Medicine*." It will be a one-day, Saturday event at a hospital in our region. This is will a unique conference on subjects that are rarely if ever discussed. Further details will be provided when I have arranged the location of the event.

The Board of Governors Meeting will be held from September 17 to 20, 2008. I will provide information about that event in the next newsletter.

I would like to introduce a new section in our newsletter named The Internist's Corner where different topics germane to the practice of internal medicine will be discussed.

This issue will focus on the following issue: "*Why Internists Should Know About Polycystic Ovary Syndrome.*"

The Internist's Corner

Why Every Internist Should Know About Polycystic Ovary Syndrome

I picked Polycystic Ovary Syndrome (PCOS) as the first article in the Internist's Corner because there is no definitive test to make this diagnosis. This is a syndrome that requires an astute, clinical decision based on a history and physical which is the essence of being an internist. I see one or more patients with this syndrome daily at my clinic who are currently undiagnosed. Early diagnosis fosters better care and possible may delay or prevent the long-term consequences.

Polycystic Ovary Syndrome (PCOS) affects approximately 5% to 10% of women. It affects women of all races and ethnicities. It has been known by a plethora of other names including Stein-Levanthol Syndrome, Chronic Hyperandrogenic Anovulation, Ovarian Hyperandrogenic Dysfunction, etc.

PCOS is not merely a reproductive disorder but the most common endocrinological disorder affecting women in their reproductive years. Although hyperandrogenism and infertility that are associated with PCOS are distressing to young women, its metabolic sequelae are far more serious for the individual in terms of morbidity and mortality. PCOS is a lifelong condition which is a harbinger of more serious sequelae such as diabetes mellitus, hyperlipidemia, endometrial hyperplasia/carcinoma, cosmetic and dermatological problems, infertility, depression and poor self-image, central obesity, sleep apnea, etc.

PCOS accounts for 95% of cases of hyperandrogenism. This syndrome is responsible for over 20% of all cases of amenorrhea. It is also responsible for up to 75% of all cases of anovulatory infertility.

There is no universally accepted definition for PCOS! However, most clinicians and organizations support the following criteria:

1. Hirsutism and/or hyperandrogenemia, plus
2. Oligo-anovulation and/or polycystic ovaries, plus
3. Exclusion of other androgen excess or related disorders

Genetic studies have identified a link between PCOS and disordered insulin metabolism, and indicate that the syndrome may be the presentation of a complex genetic trait disorder. While the precise mode of inheritance is still uncertain, a familial basis for the syndrome is well established and it is not uncommon to find a mother or sister with l or more symptoms of PCOS.

The pathogenesis is unknown with many theories suggesting a genetic trait with an environmental triggers involving the ovaries, dysregulation of steroidogenesis and insulin resistance.

Hyperandrogenism which is frequently seen in this disorder can be clinical and/or biochemical. Clinical manifestations of hyperandrogenism include the following: Hirsutism, Acne, Seborrhea, Acanthosis nigricans, Male-pattern Balding, Increased Muscle Mass (rare), Deepening Voice (rare) and Clitoromegaly (rare).

Irregular menstrual history is given by most patients and can range from fewer than 8 cycles per year to amenorrhea. It is important to note that one can have normal periods with this syndrome but may not be ovulating.

Seventy-five percent of patients with PCOS have polycystic ovaries detected by transvaginal ultrasonography, although the false-positive rate is high (approximately 25% of women in the general population have the same ovarian morphology without PCOS). The diagnosis of polycystic ovaries should not be based merely on a "polycystic" or "multicystic" appearance. At least 1 ovary should have a volume of >10cm3 (mL), or there should be >= 12 follicles measuring 2 to 9 mm in diameter. I utilize the ultrasound on these patients to check for the endometrium for hyperplasia and carcinoma.

Fifty to sixty percent of patients are centrally obese (BMI >= 30). However, there are both lean and obese PCOS patients pointing to a spectrum of disease. A hallmark of PCOS is insulin resistance out of proportion to the magnitude of obesity. In fact, lean PCOS patients still have increased insulin resistance compared to controls. It is estimated that 30% of women with PCOS who are obese have either impaired glucose tolerance or NIDDM by age 40.

Potential Long-Term Consequences associated with PCOS include the following:

- Infertility
- Obesity
- Dyslipidemia(elevated TGC and low HDL)
- Diabetes Mellitus
- Sequelae of Medical Problems with Obesity
- Endometrial Hyperplasia/ Cancer especially before the age of 30 in less than 1% of patients
- Neurological Sequelae-Obstructive Sleep Apnea and other Sleep Disorders
- Hypertension probably related to obesity rather than PCOS
- Increased risk of miscarriages, gestational diabetes and hypertension during pregnancy

With the risk factors of DM, Hyperlipidemia, HTN and Obesity, there is a concern of increased risk of coronary artery disease (CAD). Although the final verdict is not yet out, it seems from studies so far that there is not an increased risk of CAD in PCOS(? from long-term estrogen effect).

In regard to laboratory studies, it should be emphasized that the main clinical rationale for measurement of certain labs(free and total testosterone, DHEA-S, prolactin, TSH, etc) in hirsute women is to rule out more serious causes of hyperandrogenism other than PCOS. Such disorders would include congenital adrenal hyperplasia, ovarian tumor, hyperprolactinoma, etc. In hyperandrogenemia, 60% to 80% of patients may have increased circulating androgen levels, primarily free testosterone. This cannot be the sole diagnostic criterion, because 20% to 40% or more of patients with PCOS have normal androgen levels. Additionally, these androgen assays are NORTORIOUSLY INACCURATE.

Possible laboratory abnormalities seen in patients with PCOS may include the following:

- Increased free testosterone/Normal to Increased testosterone, increased androstenedione
- Increased DHEA-S, DHEA
- Increased LH, normal FH; Increased LH/FSH ratio
- Increased estradiol, estrone
- Lipid abnormalities: Increased triglyceride and decreased HDL
- Increased fasting insulin; increased 2 hour post-prandial glucose
- Increased insulin resistance
- Decreased sex hormone binding globulin
- Mildly elevated prolactin
- Increased AST,ALT in pts with NASH

For the diagnosis of PCOS, the following may be considered:

- Hx and Physical
- Pelvic Ultrasound(Transvaginal is best); Endometrial thickness should always be assessed to exclude significant endometrial pathology.
- Hormone Assays(to exclude other mimickers of PCOS)
- Glucose Testing; Glucose Tolerance Testing
- Lipid Status(to check Total Cholesterol, HDL and Triglyceride Levels)
- Other investigations
- Exclusion of other conditions that may mimic PCOS

There is a lengthy differential diagnosis for PCOS which includes the following:

- Congenital Adrenal Hyperplasia
- Androgen-Secreting Ovarian or Adrenal Tumors
- Idiopathic Hyperandrogenism
- Idiopathic Hirsutism
- Syndromes of Severe Insulin Resistance
- Hyperprolactinomia
- Thyroid Abnormalities
- Cushing's Syndrome
- Androgenic Anabolic Steroid Usage
- " Other Medications Usage :Danazol, Phenothiazines, Corticotropin or ACTH analogues, ?Valproate

In regard to the treatment of PCOS, there are several key points to consider. Nonpharmacologic measures are universally recommended. These measures include the following(Lifestyle Modification):

- Diet including seeing a dietician who is knowledgeable in PCOS
- Exercise
- Weight Reduction if the patient is obese or insulin-resistant.

Pharmacologic treatments include the following:

- oral contraceptives
- antiandrogen drugs (usually spironolactone) for hirsutism
- insulin sensitizers such as metformin (not FDA approved)
- statins in patients with dyslipidemia

When fertility is desired, one should consider the following:

- Referral to a fertility specialist
- BCPs and antiandrogens cannot be used when considering pregnancy
- Sometimes weight loss helps
- Insulin sensitizers, especially metformin (not FDA approved)
- Thiazolidinediones(not studied, ?risks)
- Fertility Drugs-clomiphene citrate, aromatase inhibitors, gonadotropin therapy, gonadotropin-releasing hormone agonists,
- Gonadotropin-releasing hormone antagonists
- Laparoscopic Ovarian diathermy
- In vitro fertilization/embryo transfer

Who should manage PCOS?

PCOS has evolved out of the purview of the reproductive specialist and gynecologist. PCOS is probably best managed by an internist, family practitioner or endocrinologist with the assistance of subspecialists including gynecologists, fertility specialist, dermatologists and in the long run, the cardiologist and oncologist as indicated.

Key Points of this Article on PCOS

- PCOS is the most common cause of anovulatory infertility.
- PCOS is one of the commonest endocrinopathies to affect women(5-10%)
- PCOS probably represents a spectrum of disease with variable presentations.

- Is important to diagnose PCOS because of the potential long-term consequences.
- Early diagnosis may delay or possible prevent some of sequelae associated with PCOS
- Further research is necessary in this syndrome

Why is PCOS unfamiliar to most Clinicians?

1. Poorly taught if it all, in medical school.
2. PCOS probably represents a spectrum of disease and variable presentations which may be elusive to the generalist or specialist.
3. There is no definitive lab test or noninvasive procedure to make the diagnosis.
4. PCOS has traditionally fallen in the realm of the gynecologist when in reality, this syndrome should involve several different types of physicians including the primary care provider/internist.
5. There is no financial advantage for drug companies to promote this syndrome since most medications used to treat this syndrome are generic.
6. There is not prominent spokeswomen with PCOS for the media.
7. And thus, the purpose of my article!

Patient Support Groups

- PCOSA-Polycystic Ovarian Syndrome Association, Inc.(Patient Support Group)
- Telephone: 877-775-PCOS
- Mail: P.O.Box 7007, Rosemont, Il 60018
- Email:info@pcosupport.org
- Internet:www.pcosupport.org

Medical Association Society for PCOS

- Androgen Excess and PCOS Society
- Irene Longo Carmina , Administrative Assistant
- via delle Croci 47, Suite 10, Palermo, 90139 Italy, Phone : +39-091328997, Fax: +39-091-6552953
- email: info@ae-society.org

For further reading, please consult the following:

1.Androgen Excess Disorders in Women: PCOS and Other Disorders, by Azziz, Nestler, Dewailly, Humana Press, 2006

2.PCOS, by Balen, Conway, Homburg, Lego, Taylor & Francis Publishers, 2005

3. PCOS, by Chang, Heindel, Dunaif, Marcel Dekker, Inc. 2002

4. PCOS, by Roy Homburg, Martin Dunitz, 2001

5.PCOS, by Gabor T. Kovac, Cambridge University Press, 2000

6.PCOS the Hidden Epidemic,by S. Thatcher, Perspectives Press, 2000

7.Androgen Excess Disorders in Women,by Azziz,Nestler,Dewailly,Lippincott-Raven,1997

In the next issue of the Governor's Newsletter, the Physician's Corner will discuss the issue of Migraines.

Thank you and success and fulfillment in your profession. Sincerely,

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Governor of the ACP, Southern California, Region II