

## NASPAG 25 Years Later



The basic foundation of gynecology begins in 1550 BC, as documented in the Papyrus Ebers in which, for the first time, there was reference to the diseases of women. The next hallmark was in the year 450 BC by Hippocrates, who was the first to develop gynecological instrumentation. We had a bit of a hiatus until the 16<sup>th</sup> century when modern gynecology, in large part as we know it today, was developed under the aegis of Caspar Wolf-Zurich. This physician developed the “Encyclopedia of Gynecology” in 1565. Operative gynecology had its early foundation in the work of James Marion Sims in the 19<sup>th</sup> century, with his ingenious development of operative tools that still have application at present.

On a parallel level, the American College (Congress) of Obstetricians and Gynecologists (ACOG) identified the need to educate physicians with respect to pediatric and adolescent gynecology. All these efforts culminated in the year 1982 when a North American chapter of the Federation Internationale de Gynecologie Infantile et Juvenile (FIGIJ) was established. The very first meeting of the North American Society of Pediatric and Adolescent Gynecology was in Washington, DC, in 1986, with the 8<sup>th</sup> International Symposium of FIGIJ. See Fig. 1. A number of founders, including Drs. Albert Altchek, David Muram, S. Jean Emans,

Donald Goldstein, Gita Gidwani, Alvin Goldfarb, Paul McDonough, and Joseph Sanfilippo were the original members of the society (Fig. 2). The second annual meeting was held at the Cleveland Clinic Foundation in 1987, under the direction of Dr. Gidwani, who served as the Program Chair.

It became rapidly obvious that there was a need for development of a journal to serve as a vehicle of communication for members of NASPAG. The first specialty journal was introduced by Sir John Dewhurst who served as Editor-in-Chief of the *Journal of Adolescent and Pediatric Gynecology* from 1988 to 1995. Sir John was elected as the youngest president of the Royal College of Obstetricians & Gynaecologists. In the hands of those he mentored, his surgical technique remains in vogue to this day.

The very first Executive Director of NASPAG was Dr. Alvin F. Goldfarb, Professor of Obstetrics & Gynecology at Jefferson Medical College. Time progressed and in 1988 the *Journal of Pediatric and Adolescent Gynecology*, as we know it now, 24 years later, was developed. Paul G. McDonough was editor-in-chief for the first year and Dr. Joseph S. Sanfilippo has been the editor-in-chief from then to this time. The Journal has a number of segments including Mini-reviews, Original studies, Case Reports Tips for Clinicians, Mental Health Corner, Surgical Challenges, Management Quandary, Opinions in Pediatric & Adolescent Gynecology, Pediatric Urology, Allied Health Professionals, and Pediatric Dermatology and well as “Teach the Teacher.” The impact factor remains very respectable for our Society Journal.

### Publication

Many times individuals have called upon the Editor-in-Chief and the Editorial Board to learn about publication of a manuscript. Allow me to provide a number of suggestions for organizing your manuscript.

- Start by developing a hypothesis – this answers a question “yes” or “no”
- State the objective clearly
- Data overview
- Itemize the results
- Create figures and tables before writing the results section
- Pay attention to Instructions for Authors in the Journal.

As reviewers read a manuscript, they are interested not only in the science but also command of the English language. To this effort, the following is suggested:



Fig. 1. 8<sup>th</sup> World Congress of Pediatric & Adolescent Gynecology, Washington DC

Use correct tense for the section:

- Abstract: past
- Introduction: present
- Materials & Methods: past
- Results: past
- Discussion: present
- Plan on multiple drafts before you submit your manuscript
- Try to be specific and avoid terms such as “if”

The abstract should focus on a number of important principles:

- Objectives & Hypothesis
- Methodology in brief
- Results – Summary
- Principal Conclusions
- Resolution of hypothesis

Limit the use of “precise clinical applications” and avoid use of “*P* value”; instead use the appropriate statistical analysis

### Introduction

- Be concise—major scope of the problem should be clearly conveyed
- Identify “gaps in the overall knowledge of the subject”
- Set the stage for why the study is important
- Briefly convey methods utilized for the investigation
- Objectives to be achieved

### Materials & Methods

- Tables are key and figures aid in clarification
- Key points should be emphasized and include information about the control population
- State statistical assessment
  - Power analysis
  - *P* values
  - Do not include results in this section

### Results

- Outline and prioritize what you and the co-authors feel are the most important points.
- Use of tables and figures helps to convey information.

- Statistically significant difference versus “biological/clinical significance”
- Reader must be able to judge the data independently

### Discussion

- The first paragraph should summarize findings
- Select 3 or 4 key topics to discuss
- Show the data
- Hypothesis has been answered “yes” or “no”
- Objectives have been achieved (this question must be addressed)
- The last paragraph should be succinct and provide proper conclusions

Ideally, a letter accompanying the manuscript suggesting 3 to 5 reviewers would be helpful to the editor (Personal Communication, M. Nelson).

### Historical Perspective

There are a number of hallmark events that have occurred in the specialty of pediatric and adolescent gynecology and they began Sept 12, 1940, when Professor Peter from Prague established the first Pediatric and Adolescent Gynecology Clinic.

- In 1941, the first textbook on the subject was written by Dr. Goodrich Shauffler.

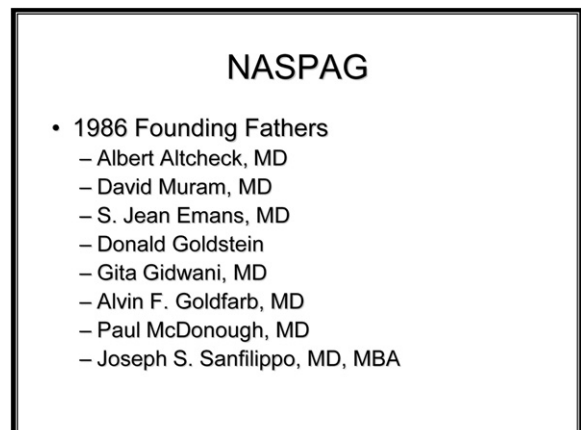


Fig. 2. Founders of NASPAG.

- In 1958, Dr. John Huffman and Dr. Vincent Capraro provided the text entitled “The Gynecology of Childhood and Adolescence.”
- The next key contribution to the specialty was in 1963, when Professor Sir John Dewhurst published a textbook entitled “Gynaecological Disorders of Infants and Children.”

#### *Setting up a Pediatric Adolescent Gynecology Unit*

As a neophyte, who has the mission to embark upon learning how to set up a pediatric and adolescent gynecology center at their particular facility, a number of suggestions can facilitate such; the first of which is to identify a team, including a nursing staff that has a particular interest in pediatric and adolescent gynecology. This individual becomes instrumental in educating patients and parents about the idiosyncrasies of the process, such as physical examinations. Actually, pediatric adolescent gynecology begins in the delivery room with examination of the external genitalia. This assessment provides an important message/signal to the parents that evaluation of the external genitalia is an integral part of the overall physical examination of the newborn. In an office setting, use of low power magnification cannot be emphasized enough and having the patient/parent involved is particularly important. In the pediatric patient, the use of frog-leg position as well as knee-chest position and having the patient involved in what I term “show and tell” approach is of paramount importance. Again use low power magnification and make every effort to get an adequate examination. If it is felt that the examination is inadequate then strong consideration to sedation and reassessment would be appropriate. If the examination has a positive outcome, and hopefully that happens, it’s important to so communicate to the patient.

#### *Specific problems in pediatric and adolescent gynecology: Polycystic Ovarian Syndrome*

The incidence of this “disease” is 4–10% of the population.<sup>1</sup> First degree relatives have an incidence of 24% and affected sisters 32%.<sup>1</sup> Zumoff et al were among the first to provide a chronobiologic assessment of luteinizing hormone secretion in teenage girls with polycystic ovary syndrome.<sup>1</sup>

The overall goal for a patient with hirsutism and/or virilization is to rule out an androgen producing tumor, or adrenal hyperplasia. Now this in part can be accomplished by obtaining serum dehydroepiandrosterone sulfate (DHEA-S) and 17 hydroxyprogesterone, if the latter is interpreted as normal, it in essence rules out ACOAH (Adult Onset Adrenal Congenital Hyperplasia) Fasting serum testosterone should be less than 200 mg per dl. When one considers the diagnosis of PCOS the circulating level of serum testosterone appears to be the most sensitive and important androgen to be evaluated and if it is greater than 2 standard deviations above the mean, it is of very important clinical significance.

In 2010, Carmina et al reported “new images of PCOS.”<sup>2</sup> These authors felt that chronic anovulation is common in

the adolescent. Menstrual irregularities occur with an incidence of 40–50% of adolescents having anovulatory cycles. More specifically, ovulatory cycles are really only established in gynecologic year one in 23–35% of patients.<sup>2</sup> By gynecologic year five, 70–80% have ovulatory cycles. So thus it is felt that “normal” is menstrual cycles that are every 40–45 days until 2 to 3 years after menarche. Now, in general, 35 days is the upper limit of normal interval in 98% of adults when it comes to “ovulatory cycles.” In adolescents 35 to 40 days is common in 66% of patients.<sup>2</sup> Irregular menses persisting 2 years after menarche is the starting point for establishing the diagnosis of PCOS in adolescence. There is more and more evidence that PCOS is an intra-uterine problem; this is manifested by elevation in cord blood androstenedione levels.

With respect to the pathophysiology of PCOS there is an increase in luteinizing hormone (LH) pulse amplitude, preferential LH secretion, GnRH pulse frequency variations and there is an increase in alpha and beta sub units of LH. This results in increased theca cell androgens, insulin resistance in the form of hyperinsulemia, metabolic defect in insulin metabolism at the ovarian level, all of which results in elevated androgens. So thus, there is an interaction between the GnRH pulse generators with pituitary release of LH at higher than normal levels, aberration at the level of the ovary with follicular development arrest which further contributes to increased androgen production by theca cells and enhanced insulin resistance and a continuous positive feedback scenario.

There is also evidence of decreased sensitivity to insulin in muscle and adipose tissue as has been communicated by Pfeifer and Kives.<sup>3</sup> These authors noted a compensatory increase in insulin level and insulin resistance (20–60%) in PCOS patients. It appears to be an insulin post-binding defect with a problem predicated at the insulin receptor signaling level. This results in tyrosine metabolic defect as opposed to the “normal” serine metabolic insulin action. There is also an increase in 17,20 desmolase activity.

So in summary with PCOS especially in the adolescent there is evidence that:

- Insulin decreases sex hormone binding globulin.
- Insulin has a direct increase on LH production.
- Insulin activates its own receptor in the ovary, adrenal, and pituitary glands.
- Insulin upregulates insulin-like growth factor (IGF-1) receptor and decreases insulin-like growth factor binding protein (IGFBP)1 which results in an increase in IGF-1 production.

The Rotterdam criteria associated with PCOS namely *viz.* irregular menses, hyperandrogenemia, increased ovarian size (> 10 cc) can only be considered in the adolescent if they are 2 years post menarche.<sup>2</sup> These patients need to be very carefully followed into adulthood for onset of PCOS.<sup>3</sup> A glucose tolerance test with 75 gram glucose load should be considered; ACOG clearly recommends this in adults. The role of hemoglobin A1c is a good screen in adults and an effort to identify those predisposed to cardiovascular disease.. The main objective with PCOS is:

- Control of menstrual function
- Control of androgen excess
- Prevention of long term metabolic disorders
- Endometrial protection

There is evidence focused on the effect of weight loss on menstrual function in adolescents with PCOS.<sup>4</sup> A study conducted by Ornstein and co-workers noted that in 24 adolescents aged 12–22 years with PCOS and BMI over the 85<sup>th</sup> percentile (35.7 kg/m<sup>2</sup>) who underwent an average weight loss of 6.5% and had an associated decrease in waist circumference of 5.7 cm, they were significantly more likely to have “improved menstrual function.” This once again attests to the importance of lifestyle and a weight control exercise program for our adolescents.

#### Chronic Pelvic Pain

The next area to be considered is that of adolescent chronic pelvic pain, specifically work by Song and Advincula published in the *Journal of Pediatric and Adolescent Gynecology*.<sup>5</sup> They identified that, in the patient with chronic pelvic pain, which was defined as 6 or more months refractory to medical therapy, the laparoscopic findings included:

- a normal pelvis in 25–40%
- endometriosis in 38–45%
- ovarian cysts in 2–5%
- uterine malformation in 5–8%
- evidence of pelvic inflammatory disease in 5–15%<sup>4</sup>

Whenever a clinician is faced with pelvic pain, especially recurrent pelvic pain in the adolescent, it is very important to consider the distinct possibility of a müllerian anomaly and thus the importance of obtaining pelvic sonographic assessment. The pelvic pain may present as cyclic or acyclic pain. The traditional theories of Samson, müllerian rests, increased endometrial cell apoptosis, increased matrix metalloproteinase activity, and peritoneal cavity angiogenesis pervade as related to development of endometriosis. A number of patients have an associated GI etiology for pain and this must also be considered in this patient population. Complementary and alternative (holistic) management should also be given due consideration; this would include behavior modification, relaxation, biofeedback, improving coping skills, and physical therapy as well as acupuncture.<sup>5,6</sup>

Thus with respect to summarizing chronic pelvic pain the following systems should always be considered: GI, GU, Gyn, and Musculoskeletal.

It is not uncommon for an adolescent to be “the victim of chronic constipation” and this must always be considered in the differential. Irritable bowel syndrome must be in the differential diagnosis.

#### Oncofertility

The last and indeed extremely important communication to be focused on is oncofertility in the pediatric and adolescent patient. Clinicians must be clearly aware of the

potential gonadal toxicity, especially of alkylating agents such as cyclophosphamide, busulfan, plant alkaloids (vinca alkaloids), and other agents, e.g. anti-folates, that have a profound adverse effect on oocyte activity. High-dose (6–10 Gy) radiation therapy is equated with a 95% sterilization rate.<sup>9</sup>

So what is your obligation as a clinician? Simultaneous administration of gonadotropin releasing hormone agonists (GnRHag) and co-treatment with chemotherapy has the potential to create a hypogonadotropic effect which may decrease utero-ovarian perfusion and thus preserve subsequent ovarian function. The problem here is that the effectiveness of GnRH agonist therapy is limited. Prospective data utilizing Zoladex, a GnRH agonist, versus placebo prescribed as co-treatment with chemotherapy is associated with a 69% resumption in spontaneous ovulation in the treatment group versus the placebo group in which it was 26%. The bottom line is that there may be “some degree of protection” with simultaneous administration of GnRH agonist with chemotherapy.<sup>7</sup>

Other approaches include ovarian transposition, i.e. oophoropexy where the ovaries are suspended out of the field of radiation. The typical example might be a patient who has a sacral tumor, i.e., sacral malignancy and in need of radiation therapy. Cryopreservation of the ovary remains of interest; a study from New Zealand focused on fertility preservation prior to initiation of chemotherapy in 47 prepubertal girls.<sup>8</sup> More commonly this is administered to patients with acute myelogenous leukemia, acute lymphocytic leukemia, chronic myelogenous leukemia, and lymphoma sarcoma. Oocyte cryopreservation when associated with in vitro maturation remains in its infancy. Embryo cryopreservation in couples prior to embarking upon chemotherapy remains the most efficacious means of future fertility preservation.

#### Summary

The sub-specialty of pediatric and adolescent gynecology has come such an incredibly exciting long way over the past 25 years. Being part of NASPAG affords you the opportunity to be part of a community and/or committee



Fig. 3. Committees of NASPAG.

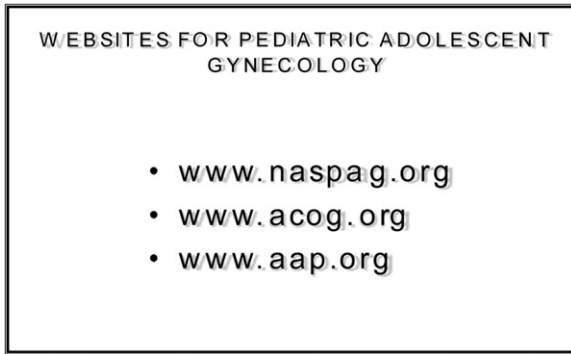


Fig. 4. Websites for Pediatric/Adolescent Gynecology.

(Fig 3). We currently have eight fellowship programs in North America. We continue to have ever increasing number of attendees at our annual clinical and research meeting and the ability to provide preventive health care for adolescents, to educate them with respect to preventive care, such as safe sex, date rape prevention, the hazards of substance use/abuse, tobacco ramifications, short and long term, and the bottom line is that primary care physicians at all levels, whether pediatricians, family practitioners, or obstetricians and gynecologists should incorporate pediatric and adolescent gynecology into their clinical armamentarium. This can be relatively easily accomplished with use of tool kits for adolescent gynecology, ped-gyn clinical scenarios and a number of other readily available tools. The reader is directed to the websites for Pediatric & Adolescent Gynecology listed in Fig. 4.

I thank you for your attention and it continues to be my privilege to serve as Editor-in-Chief of the *Journal of Pediatric and Adolescent Gynecology* and Executive Director of the North American Society for Pediatric and Adolescent Gynecology. I wish you every success in your career and am hopeful that you will “tell your friends” about all the advantages of being actively involved in pediatric and adolescent gynecology.

Joseph S. Sanfilippo  
Editor-in-Chief

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