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OBGYN NEWS

Promoting Excellence In
Women's Healthcare In Georgia



An Update on Polycystic Ovarian Syndrome (PCOS)

Lauren Rouleau, MD, PhD and
Leslie Adams, BS, MD

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder affecting up to 10-18% of women.[1] The clinical manifestations are oligo or amenorrhea (typically less than 9 menstrual cycles per year), evidence of hyperandrogenism (physical or biochemical), and polycystic ovarian morphology on ultrasound ("string of pearls" appearance). The Rotterdam criteria, developed in 2003, requires at least 2 of the 3 aforementioned criteria.[2] The pathophysiology of PCOS is multifactorial and not entirely elucidated.[3] Beyond hyperandrogenism and insulin resistance, recent research has implicated neuroendocrine factors resulting in dysregulation of the hypothalamic-pituitary-ovarian axis as major contributors to the pathophysiology.[4, 5]

Recently, the classification of ovulatory disorders has been updated. In place of the "PALM-COEIN" classification system, FIGO has proposed a new, tiered system, beginning with four overarching sources of ovulation dysfunction characterized by the mnemonic "HyPO-P:" hypothalamus, pituitary, ovary, and PCOS.[6] This new classification system gives PCOS its own designation within ovulatory disorders, which is a notable change as it previously was included in the "other" category. In separately classifying PCOS, it recognizes the syndrome as a common and important cause of ovulatory dysfunction.

PCOS is a diagnosis of exclusion,

and other causes of hyperandrogenism and ovulatory dysfunction must be ruled out before a patient can be diagnosed. The Rotterdam criteria, developed in May 2003 at the Rotterdam PCOS Consensus Workshop, continue to be the more commonly utilized diagnostic criteria, over the NIH criteria (1990) and the Androgen Excess Society criteria (2006).[2] The Rotterdam criteria have been shown to encompass the major 4 phenotypes of PCOS, with classical PCOS (meeting all three criteria) being the most common.[7] Another phenotype of note is lean PCOS, characterized as patient meeting criteria for PCOS diagnosis, exclusion of other diagnoses, and having a BMI <25. Diagnosis of lean PCOS is incredibly important, as patients with lean PCOS have many of the same risk factors for long-term health sequelae as patients with classical PCOS phenotype.

Treatment of PCOS mainly depends on a patient's current goals and symptoms. Lifestyle modifications via weight loss and implementation of regular exercise are the mainstay of treatment to improve symptoms and reduce long-term health consequences. For patients with ovulatory dysfunction who are not actively seeking pregnancy, combined low-dose oral contraceptives are a useful treatment.[8] Metformin can be a useful adjunct to improve insulin resistance, decrease symptoms of hyperandrogenism, and improve ovulatory function, but may not be appropriate for all patients and is not specifically approved by the FDA for this

use. For patients with hirsutism, laser or manual hair removal is a standard non-pharmacologic management option. If patients have recurrent hair growth or prefer pharmacologic therapy and are not seeking pregnancy, antiandrogens or spironolactone are the primary recommended agents. Use of these agents are recommended in combination with OCPs due to their potential teratogenicity. Other options for treatment of hirsutism include flutamide, an androgen-receptor antagonist, finasteride, a 5-alpha reductase inhibitor, or topical eflornithine, an ornithine decarboxylase inhibitor.[8]

Infertility is a common and important sequela of PCOS. Lifestyle optimization is imperative to improving fertility prior to conception. Letrozole is considered the first-line treatment in ovulation induction (OI) for PCOS-related infertility.[9] In-vitro fertilization (IVF) is another treatment option for patients who have failed OI. Patients with PCOS must be monitored closely during gonadotropin stimulation, as they are at risk for developing ovarian hyperstimulation syndrome (OHSS) due to high antral follicle counts at baseline. Metformin may be useful to help mitigate the risk of OHSS in this population.[10]

Patients with PCOS must be regularly monitored for development of other comorbidities. Cardiometabolic disease, including cardiovascular disease, type II diabetes, dyslipidemia, and metabolic syndrome, as well as depression and anxiety are particularly common in

(Continued on pg. 11)



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QUICK LINKS



AWARENESS CAMPAIGNS

FOR THE MONTHS OF

August and September

August

NATIONAL BREASTFEEDING MONTH and WORLD BREASTFEEDING WEEK



Breastfeeding is the best source of nutrition for most infants. It can also reduce the risk for certain health conditions for both infants and mothers. Most mothers want to breastfeed but stop early due to a lack of ongoing support. To learn more, don't miss our featured **breastfeeding article and resources on page 8** and visit <https://www.cdc.gov/breastfeeding/index.html>.

September

OVARIAN CANCER AWARENESS MONTH

Ovarian cancer causes more deaths each year than any other gynecologic cancer in the U.S. In 2019, the latest year for which incidence data are available, in the U.S., 19,571 new cases of ovarian cancer were reported among women, and 13,445 women died of this cancer. For every 100,000 women, 10 new Ovarian cancer cases were reported and 6 women died of this cancer. To learn more, don't miss our featured article "**Ovarian Cancer Update**" on page 10 and visit <https://www.cdc.gov/cancer/ovarian/index.htm>



POLYCYSTIC OVARIAN SYNDROME (PCOS) MONTH

Polycystic ovary syndrome happens when a woman's ovaries or adrenal glands produce more male hormones than normal. One result is that cysts (fluid-filled sacs) develop on the ovaries. Women who are obese are more likely to have PCOS. Women with PCOS are at higher risk of diabetes, metabolic syndrome, heart disease, and high blood pressure. To learn more, don't miss our featured article

"**An Update of PCOS**" on page 1 and visit:

<https://medlineplus.gov/polycysticovarysyndrome.html>

SEXUAL HEALTH AWARENESS MONTH

The World Health Organization defines sexual health as a state of physical, emotional, mental and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction or infirmity. Sexual health requires a positive and respectful approach to sexuality and sexual relationships, as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination and violence. Learn more at:

<https://www.cdc.gov/sexualhealth/>



WORLD HEART DAY (September 29th)

World Heart Day is a global campaign during which individuals, families, communities and governments around the world participate in activities to take charge of their heart health and that of others. To learn more, don't miss our featured article "**Postpartum Care of Patients with Complicated Pregnancy**" on page 5 or click on the link below to download a campaign toolkit: <https://world-heart-federation.org/world-heart-day/>

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Postpartum Care of Patients with Complicated Pregnancy

Alexis Cutchins, MD and M. Carolina Gongora, MD



Hear disease is the number one cause of death in women older than 65 in the United States but only 56% of women in the US recognize heart disease as their number one killer. 40% of women who have a myocardial infarction die within one year from cardiac complications and most of these women have no prodromal symptoms. Pregnancy related complications such as gestational diabetes, fetal growth restriction, gestational hypertension, pre-eclampsia, and chronic hypertension can result in a higher risk of cardiovascular disease later in life¹. Preeclampsia is associated with a 4-fold increase in future incident of heart failure and a 2-fold increased risk of coronary disease, stroke and death due to cardiovascular cause². Pregnancy offers a unique opportunity to recognize women who may be at risk for heart disease in the future. By recognizing these patients and referring them to internal medicine or cardiology at discharge from the hospital or at their post-partum follow up appointment we can help them define the risk of cardiovascular disease or sometimes even detect undiagnosed cardiovascular disease. Early diagnosis is key in providing prevention of heart disease and stroke in these women.

For women with a diagnosis of high blood pressure (BP) or heart disease it is advised to have a post-partum follow up visit within 10-14 days of delivery. At the post-partum check-up it is useful to check and document BP and heart rate. Refer to cardiology or internal medicine for further evaluation and recommendations. The patient will be counseled on their cardiovascular risk by taking biometric measurements and performing blood work. They will be given tools to help them follow a low sodium, heart healthy diet (Mediterranean). Exercise is encouraged in this population of patients once cleared post-partum by OB.

Once the patient has finished breastfeeding they will have fasting lipids checked to further risk stratify. Other potential risk factors like smoking, obesity, diabetes and family history of heart disease will be documented and addressed.

If during the follow up visit patient is found to be hypertensive there are some steps that can be taken prior to referring them to an internist or cardiologist. The patient should follow a low sodium diet, less than 2000 mg sodium daily. It is helpful to instruct the patient to keep a log of her BPs. Proper BP measurement technique should be explained. BP should be measured while sitting in a relaxed place for 5 minutes with both feet on the ground. BP can be taken at various times of day and noted in a log with the time and date so these measurements can be reviewed at the patient's visit with cardiology. At the initial visit with an internist or cardiologist medications may be added after a review of the home BP log. An ECG will be performed and based on that, and the patient's history, other testing may be indicated.

Peripartum cardiomyopathy can occur up to five months after giving birth. It is much rarer (about 1,000 cases a year diagnosed in the US, Canada and Europe) but should be on the radar of any OB/GYN. Screening for symptoms at post-partum follow up is important. This would include questions like:



- Are you newly retaining fluid?
- Do you have shortness of breath when you lie flat?
- Do you wake up in the middle of the night gasping for air?
- Are you having more difficulty performing your daily activities?

While it may be hard to tease out what symptoms are secondary to lack of sleep and caring for a newborn and what symptoms are related to cardiomyopathy and heart failure these questions might help. If suspicion for cardiomyopathy patient should be referred to a cardiologist who will likely get an echocardiogram. Labs such as BNP, CMP, TSH and CBC are also helpful.

Treating risk factors for heart disease and optimizing prevention strategies is the best thing we can do to decrease future risk of heart attacks and strokes in our patients. By recognizing these risk factors early and educating our patients we can make a huge difference on the impact of cardiovascular disease in women.

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2018-2020

MATERNAL MORTALITY REPORT



2018 – 2020 Executive Summary

KEY PIECES OF INFORMATION

- There were **30.2 pregnancy-related deaths per 100,000 live births**.
- The leading causes of death were **hemorrhage, mental health conditions, cardiomyopathy, cardiovascular and coronary conditions, embolism, and preeclampsia and eclampsia**.
- Of the pregnancy-related deaths, **89% had at least some chance of being prevented**.
- Of the pregnancy-related deaths occurring after delivery, **60% were insured by Medicaid at the time of delivery**.

Of note, in keeping with evolving case review guidance from the CDC, there were changes made to MMRC processes since the reviews began in 2012. Therefore, data presented in this report **cannot be directly compared to previous years**.



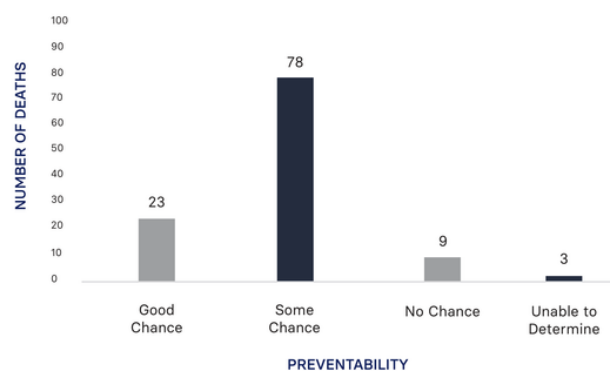
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PREVENTABILITY

A death is considered preventable if the committee determines that there was at least some chance of the death being averted by one or more reasonable changes to patient, family, provider, facility, system, and/or community factors. Between 2018-2020, 101 (89%) of the 113 pregnancy-related deaths had at least some chance of being prevented.

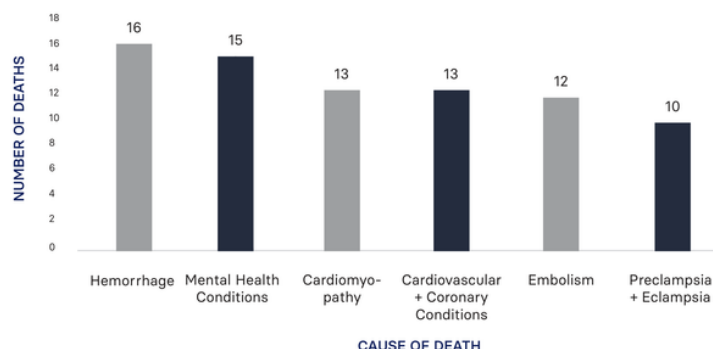
Figure 7 Chance to Alter Outcome of Pregnancy-Related Deaths Georgia, 2018-2020 (n=113)



LEADING CAUSES OF DEATHS PREGNANCY-RELATED 2018-2020

Between 2018-2020, 79 (70%) of the 113 pregnancy-related deaths were due to one of the six leading causes of death: hemorrhage, mental health conditions, cardiomyopathy, cardiovascular and coronary conditions, embolism, preeclampsia and eclampsia. The remaining 34 (30%) pregnancy-related deaths were due to seizure disorders, metabolic/endocrine conditions, anesthesia complications, blood disorders, cerebrovascular accident, homicide, infection, malignancies, renal disease, unintentional injury, and unknown cause of death.

Figure 8 Leading Causes of Pregnancy-Related Deaths
Georgia, 2018-2020 (n=79)



The leading causes of pregnancy-related death were hemorrhage (16; 14%), mental health conditions (15; 13%), cardiomyopathy (13; 12%), cardiovascular and coronary conditions (13; 12%), embolism (12; 11%), and eclampsia and preeclampsia (10; 9%).

CAUSE OF DEATH VARIATIONS WITHIN RACE / ETHNICITY SUBGROUPS

Between 2018 and 2020, cardiomyopathy (10; 16%) and embolism (9; 14%) were the leading causes of death among non-Hispanic, Black women. Mental health conditions (10; 27%) and hemorrhage (8; 22%) were the leading causes of death for non-Hispanic, White women.

TABLE 4 Leading Causes of Pregnancy-Related Deaths Among Non-Hispanic, White Women Georgia, 2018-2020

CAUSE OF DEATH	NUMBER	PERCENTAGE
Mental Health Conditions	10	27%
Hemorrhage	8	22%
Cardiovascular + Coronary Conditions	4	11%
Cardiomyopathy	3	8%
Embolism	3	8%

*Table 4 includes the 5 leading causes of underlying death among non-Hispanic, White women. This table does not represent all underlying causes of death among non-Hispanic, White women.

TABLE 5 Leading Causes of Pregnancy-Related Deaths Among Non-Hispanic, Black Women Georgia, 2018-2020

CAUSE OF DEATH	NUMBER	PERCENTAGE
Cardiomyopathy	10	16%
Embolism	9	14%
Cardiovascular + Coronary Conditions	8	13%
Preeclampsia + Eclampsia	8	13%
Hemorrhage	7	11%

*Table 5 includes the 5 leading causes of underlying death among non-Hispanic, Black women. This table does not represent all underlying causes of death among non-Hispanic, Black women.



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Feed Longer and Wean Later: Extended Breastfeeding Can Boost Maternal Health Benefits

Keisha Callins, MD, MPH



In July 2023, American College of Obstetrics and Gynecology (ACOG) issued a Practice Advisory to update the duration of breastfeeding, in agreement and in alignment with the American Academy of Pediatrics' (AAP's) 2022 Technical Report with updated guidance documenting the immediate and extended benefits of the breastfeeding for the lactating parent and child. The AAP update to breastfeeding guidelines was the first time in 10 years and is a substantial change from the previous recommendation for infants to be exclusively breastfed for the first 6 months with continued breastfeeding while introducing appropriate complementary foods for 1 year or longer.

The updated guidance, which is largely supported by the World Health

breastfeeding for greater than 12 months associated with decreased risk of chronic diseases (diabetes and hypertension), and cancer (mainly breast and ovarian, but also endometrial and thyroid). While the most benefit may be noted with exclusive breastfeeding, there is no doubt that there is some risk reduction benefit with any breast feeding and increasing benefit with greater than 12 months. Conversations regarding fertility, contraceptive use, tandem breastfeeding, and nutrition will need to be a part of ongoing maternal care discussions around sustained breastfeeding.

In addition to the known benefits of breastfeeding and the impact on a child's future health including risk of obesity, hypertension, and diabetes;

ensure that all women receive optimal breastfeeding support during prenatal care, during their maternity stay, and after birth. "Unfortunately, 60% of mothers in the United States report that they do not breastfeed as long they intended to, citing issues with latch, the infant's weight, or concerns about medications. Therefore, obstetrician-gynecologists are uniquely positioned to enable lactating mothers to achieve their infant feeding goals by assessing and addressing common breastfeeding challenges as outlined in the 1st breastfeeding-related ACOG Committee Opinion February 2021.

ACOG recommends that advocacy for personal parenting choices regarding sustaining lactation should be supported by policies that impact the workplace

"AAP identifies stigma, lack of support and workplace barriers as obstacles that hinder continued breastfeeding and, along with ACOG, advocates for improved policies supporting breastfeeding initiation and ongoing support."

Organization (WHO), in summary, in addition to exclusive breastfeeding for approximately six months after birth; continued breastfeeding, along with appropriate complementary foods introduced at about 6 months, as long as mutually desired by mother and child for 2 years and beyond. This guidance will increase education among the healthcare team and encourage awareness in communities to embrace the evidenced-based recommendations and subsequent shift in cultural norms that will advance our efforts to support the mother-child dyad, and their support systems as outlined in the 2nd breastfeeding-related ACOG Committee Opinion in February 2021.

Studies and meta-analyses have found maternal health benefit with

sustained breastfeeding for two years or beyond has a lasting effect on the parent child attachment well into childhood. Lactating parents would also benefit greatly from hearing about optimizing infant nutrition for neurodevelopment and overall infant health in the first in the first 1000 days, from their obstetrician-gynecologist and other maternal health providers.

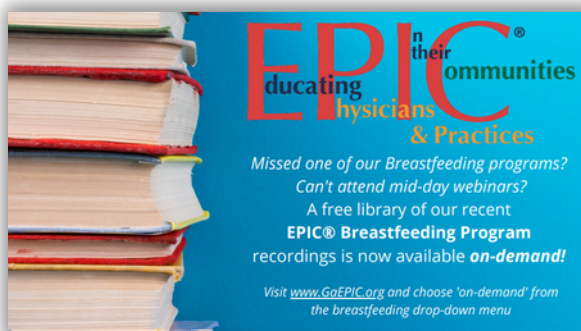
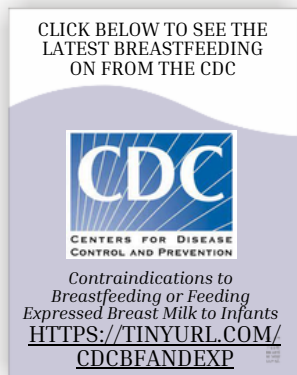
In terms of health equity, while "none of the Healthy People 2020 objectives for breastfeeding were met for non-Hispanic Black Mothers and infants among the 2018 birth cohort", we have evidence that targeted interventions such as "Ten Steps to Successful Breastfeeding" were shown to decrease the disparities in breast-feeding and have shown improvement in breastfeeding initiation and duration rates among groups with lower breastfeeding rates.

According to ACOG Committee Opinion October 2018, more work is needed to

and healthcare environments, and furthermore, efforts should be individualized to address social determinants and operationalized to overcome societal barriers. National progress has been made with the recent enactment of the December 2022 Federal PUMP Act, and here at home in Georgia, we can proudly celebrate that we are known to have some of the most progressive lactation accommodation laws in the United States. However, additional federal legislation and insurance-mandated lactation infrastructure will be necessary to further support breastfeeding beyond the first year.

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On-Demand Webinar from the June 29th 'Perspectives on Nursing, and Weaning the Older Baby, and Toddler'

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The last several years have seen exciting developments in the prevention and treatment of ovarian cancer. Ovarian cancer incidence rates decreased 1-2% per year from 1990 to 2010 and decreased even further at 3% per year from 2015 to 2019. This notable decline in incidence likely stems from widespread use of oral contraceptives and increased uptake of opportunistic salpingectomy. Despite these advancements, ovarian cancer still ranks as the fifth leading cause of cancer death in women. The American Cancer Society estimates that there will be 19,710 cases and 13,270 anticipated deaths in 2023^[i] from ovarian cancer in the US.

Origin of Ovarian Cancer and Its Prevention

While ovarian, fallopian tube, and primary peritoneal cancers are often lumped together, about 65% of the most common form of high-grade serous “ovarian” cancer appears to originate from the fallopian tube^[ii] where it progresses from precancerous lesions to cancer. These microscopic cells then disseminate into the peritoneal cavity and implant as metastatic lesions on the ovaries, omentum, and other structures, which explains the 70-80% rate of late stage at diagnosis.

Despite extensive research, there is still not an effective ovarian cancer screening test, another contributing factor to the rate of late stage diagnosis. In fact, the USPSTF, ACOG, and the Society of Gynecologic Oncology (SGO) have strongly recommended against ovarian cancer screening because it has not been proven effective in improving outcomes and may be harmful to women^[iii]. This lack of screening, coupled with our new understanding of the origin of “ovarian” cancer, has led researchers and clinicians to embrace the practice of opportunistic salpingectomy. The SGO and ACOG^[iv] have strongly promoted this practice for patients who have completed childbearing and are undergoing other pelvic surgeries like C-section, hysterectomy, or tubal ligation. Early research^[v] has already shown a substantial decrease in expected rates of ovarian cancer in these patients.

Genetics of Ovarian Cancer

Almost 24% of ovarian cancer stems from inherited cancer predisposition syndromes (e.g., BRCA mutations). It is important to identify these individuals and consider Cascade genetic testing of these patients and high-risk families^[vi]

to allow implementation of proven and effective risk reduction measures. In 2014, the SGO released a Clinical Practice Statement^[i] which recommended that all patients with ovarian cancer undergo germline genetic testing. In one recent study^[ii], ovarian cancer ranks second amongst all malignancies for the rate of germline genetic testing, but at 38.6% this still falls short of the goal of 100%.

Surgical Treatment

Cytoreduction (or debulking) surgery remains a mainstay of the treatment paradigm for ovarian cancer. Several studies^[iii] have shown the non-inferiority of administering chemotherapy prior to cytoreductive surgery (neoadjuvant chemotherapy or NACT) compared to upfront surgery followed by chemotherapy in advanced (Stage III-IV) ovarian cancer. Specifically, NACT provides essentially equivalent oncologic outcomes, with decreased postoperative morbidity and mortality. These data have substantially influenced trends in ovarian cancer treatment^[iv], with 18% of patients receiving NACT in 2006 compared to 45% in 2016, with a 10% annual increase from 2010 to 2016.

Targeted therapies

The development of poly-ADP ribose polymerase (PARP) inhibitors has revolutionized the treatment of ovarian cancer. These oral medications are given to select patients after completion of chemotherapy and are taken daily for up to two years. The positive impact of PARP inhibitors on both progression-free and overall survival is most notable in patients with germline or somatic BRCA mutations as well as homologous recombination deficient (HRD) tumors, as determined through tumor-specific testing. Most notably, the SOL01^[v] and PRIMA^[vi] trials have shown remarkable improvements in overall survival. 67% of BRCA patients treated with olaparib in the SOL01 trial were still alive at 7 years, compared to only 46.5% who received placebo.

The most recent FDA-approval for the treatment of platinum-resistant ovarian cancer is mirvetuximab soravtansine. Platinum resistance is seen in those

patients who progress within six months of receiving platinum-based chemotherapy, and it remains the deadliest and most difficult to treat type of epithelial ovarian cancer. This antibody-drug conjugate (ADC) targets a folate receptor that is expressed in a large proportion of ovarian tumors, and showed a 32% response rate^[vii].

Areas of ongoing research and challenges

Ovarian cancer research continues to expand and grow in exciting ways. Investigators are starting to look at how more women could undergo opportunistic salpingectomy at the time of non-gynecologic abdominal surgeries, such as appendectomy. In premenopausal women with BRCA1 mutations, the safety and feasibility of risk-reducing salpingectomy before bilateral salpingo-oophorectomy is being examined. Furthermore, the treatment of homologous recombination proficient (or HRD negative) tumors is a growing focus for novel therapies, as these patients do not see nearly the impact in survival from PARP inhibitors.

Takeaways for the General Obstetrician/Gynecologist

While still a leading cause of cancer deaths in women, ovarian cancer is a preventable, diagnosable, and potentially very treatable malignancy. Paying close attention to even vague abdominal and GI symptoms and ordering appropriate imaging and labs can be life saving. Performing salpingectomy at the time of other pelvic surgeries should continue to become standard of care. It is also important to routinely ask all patients about their cancer history (particularly, breast, ovarian, pancreatic, uterine and colon) and refer to genetic counseling/testing to identify high risk patients and their families. And once referred to gynecologic oncology, there are myriad tools at our disposal to optimize outcomes for our patients.

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*Portions of this article were previously published on the American College of Surgeons website in an article entitled “Surgeons Can Reduce Impact of Ovarian Cancer by Promoting Opportunistic Salpingectomies” by Dr. Susan Modesitt, MD (Leach/Hendee Endowed Professor, Director of Gynecologic Oncology Division, Emory University) <https://www.facs.org/for-medical-professionals/news-publications/news-and-articles/acs-brief/march-14-2023-issue/surgeons-can-reduce-impact-of-ovarian-cancer-by-promoting-opportunistic-salpingectomies/>

An Update on Polycystic Ovarian Syndrome

(Continued from page 1)

these patients and can have significant long-term health consequences. Regular evaluation of blood pressure, fasting lipids, hemoglobin A1C (or 2 hour oral glucose tolerance test), waist circumference, weight, PHQ-9 and GAD-7 scores are important and allow for quick identification and early intervention of these comorbidities. Other associated medical problems to be aware of include sleep apnea, eating disorders (particularly binge-eating subtype), endometrial hyperplasia or endometrial cancer, and non-alcoholic fatty liver disease. Routine screening for endometrial hyperplasia/cancer and non-alcoholic fatty liver disease is not recommended by ACOG, but may be indicated in these patients and should be performed on a case by case basis.[8]

Key points:

- PCOS is a diagnosis of exclusion and other causes of hyperandrogenism should be ruled out
- Infertility is common and letrozole is the ovulation induction agent of choice
- Many comorbid conditions are associated with PCOS and screening is essential

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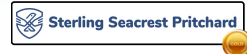
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