

# PCOS IN ADOLESCENTS DOES IS IT EXIST?

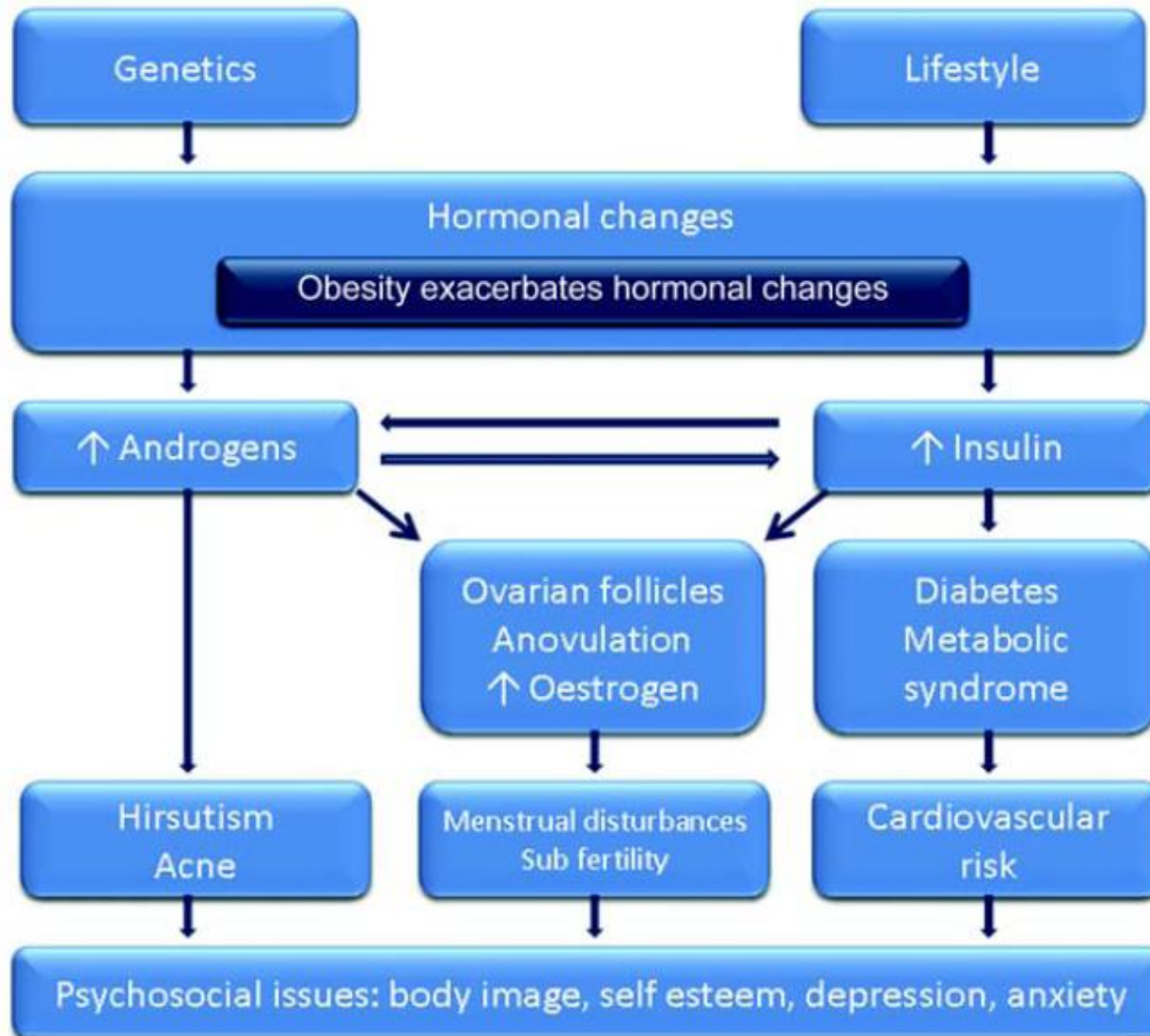
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DEPARTMENT OF PEDIATRICS AND ADOLESCENTS



Hôpitaux  
Universitaires  
Genève

Figure 1. The aetiological, hormonal and clinical features of polycystic ovary syndrome



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# PCOS - A LIFE LONG DISEASE

## PCOS: changing women's health paradigm



(young age)

- menstrual disorders
- hirsutism
- contraception
- sexual health
- infertility



(older age)

- pregnancy complications
- quality of life
- type 2 diabetes
- cardiovascular disease
- cancer risk?

The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group; Human Reproduction, Vol.27, No.1 pp. 14–24, 2012

# Dana 14.5

- Presents with oligomenorrhea for the past 3y
- Moderate acne on face and shoulders, without excessive hair.
- Struggles with weight
- Exercises 2-3 a week.
- Not sexually active.

# IMPORTANCE OF DIAGNOSIS

METABOLISM CLINICAL AND EXPERIMENTAL 64 (2015) 539–553



Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

## Metabolism

[www.metabolismjournal.com](http://www.metabolismjournal.com)



## Adolescent Oligomenorrhea (Age 14–19) Tracks Into the Third Decade of Life (Age 20–28) and Predicts Increased Cardiovascular Risk Factors and Metabolic Syndrome



Charles J. Glueck<sup>a,\*</sup>, Jessica G. Woo<sup>b</sup>, Philip R. Khoury<sup>b</sup>, John A. Morrison<sup>b</sup>, Stephen R. Daniels<sup>c</sup>, Ping Wang<sup>a</sup>

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<sup>c</sup> Children's Hospital Denver CO

**Principal conclusions.** Menstrual patterns track from adolescence to young adulthood, and oligomenorrhea predicts MetS and IFG + T2DM. Patterns of menses delays in adolescence should be considered as a significant risk factor for future development of young adult IFG + T2DM, MetS, oligomenorrhea, and polycystic ovary syndrome.

# IMPORTANCE OF DIAGNOSIS

J Clin Endocrinol Metab, April 2015, 100(4):1537–1543

## Adolescent Polycystic Ovary Syndrome Due to Functional Ovarian Hyperandrogenism Persists Into Adulthood

Robert L. Rosenfield, David A. Ehrmann, and Elizabeth E. Littlejohn

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human  
reproduction

ORIGINAL ARTICLE *Reproductive epidemiology*

## Irregular menstruation and hyperandrogenaemia in adolescence are associated with polycystic ovary syndrome and infertility in later life: Northern Finland Birth Cohort 1986 study

S. West<sup>1</sup>, H. Lashen<sup>2</sup>, A. Bloigu<sup>3</sup>, S. Franks<sup>4</sup>, K. Puukka<sup>5</sup>, A. Ruokonen<sup>5</sup>, M.-R. Järvelin<sup>3,6,7,8,9</sup>, J.S. Tapanainen<sup>1,10</sup>, and L. Morin-Papunen<sup>1,\*</sup>

Human Reproduction, Vol.29, No.10 pp. 2339–2351, 2014

# Prevalence of polycystic ovary syndrome in adolescents

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## UNDERDIAGNOSIS

**Objective:** To investigate the prevalence of polycystic ovary syndrome (PCOS) in adolescents and its association with obesity.

**Design:** Cross-sectional study using electronic medical records.

**Setting:** Not applicable.

**Patient(s):** Adolescents aged 15–19 years (n = 137,502).

**Intervention(s):** None.

**Main Outcome Measure(s):** PCOS diagnosed or defined according to National Institutes of Health (NIH) criteria.

**Result(s):** The prevalence of a confirmed diagnosis of PCOS was 0.56%, which increased to 1.14% when undiagnosed cases with documented symptoms qualifying for PCOS according to NIH criteria were included. Compared with normal/underweight girls, the

**Half** of patients with PCOS symptomatically remained **under diagnosed**.

Likelihood of receiving a **diagnosis of PCOS is higher in obese patients**.

*J Pediatr Adolesc Gynecol* 26 (2013) 234–238

Original Study

## Differences in the Management of Adolescents with Polycystic Ovary Syndrome across Pediatric Specialties

Bethany Auble MD<sup>1</sup>, Deborah Elder MD<sup>1</sup>, Andrea Gross MD<sup>2</sup>, Jennifer B. Hillman MD<sup>3,\*</sup>

Failure in diagnosis of PCOS occurred in 38% of Pediatric endocrinology clinics; and in 20% of Adolescent Medicine and PAG clinics.

**High prevalence of failure in early detection of PCOS in young patients**

- Caution should be taken before diagnosing PCOS without longitudinal evaluation.

*Witchel et al. The diagnosis of PCOS in adolescences. Clinical practice Committee Publication  
Hormone Research in pediatrics; 2015;83;376-389*

- During the transition of girls into adulthood, several features may be in evolution or may only be transitory findings

*Carmina E, Oberfield SE, Lobo RA. The diagnosis of PCOS in adolescents.  
Am J Obstet Gynecol 2010;203:201–5.*



## **INCORRECT DIAGNOSIS IN ADOLESCENCE**

- Unnecessary treatments
- Psychological distress regarding body image and infertility
- Jeopardize clinical and basic studies

## **CORRECT & EARLY DIAGNOSIS IN ADOLESCENCE**

- Start treatment and preventive measures during the adolescent years.

# CLINICAL QUESTIONS

## 1. Diagnostics in adolescentes

- Alerts of PCOS in adolescents
- Anovulation
- US criteria
- Hyperandrogenism

## 2. Investigation

## 3. Attitude

# Q1 Alerts of PCOS in adolescents

- Family History
- Low-birth Weight (LBW)
- Premature Pubarche (pubic hair <8 yo)
- Timing of menarche (9-16 yo)
- Small for gestational age (SGA)
- Other possible markers: IGF-1: LH/FSH ratio:  
AMH

*Adolescence and polycystic ovary syndrome: current concepts on diagnosis and treatment*  
*P. M. Spritzer, A. B. Motta; Int J Clin Pract, November 2015, 69, 11, 1236–1246*

# Q1 TIMING OF DIAGNOSIS

In adolescent, at what time point after onset of menarche do irregular cycles indicate ongoing menstrual dysfunction ?

# MENSTRUAL IRREGULARITIES

- Majority of adolescents establish a menstrual interval of 20–45 days within the first 2 years after menarche.
- Menstrual intervals persistently < 20 days or >45 days in individuals 2 or more years after menarche are evidence of oligo-anovulation.
- Menstrual intervals > 90 days are rare & require further investigation regardless of years after menarche.

# Q1 TIMING OF DIAGNOSIS

50% with oligomenorrhea or 2° amenorrhea are affected by a permanent ovulatory disorder.

*Wiksten-Almstromer M, Hirschberg AL, Hagenfeldt K. Prospective follow-up of menstrual disorders in adolescence and prognostic factors. Acta Obstet Gynecol Scand 2008;87:1162–8.*

Amenorrhea by age 15 years or by more than 2–3 years after telarche regardless of chronologic age is statistically uncommon and warrants evaluation and consideration of diagnoses such as PCOS (Level B).

*Witchel et al. The diagnosis of PCOS in adolescences. Clinical practice Committee Publication Hormone Research in pediatrics; 2015;83;376-389*

# RISK FACTORS FOR PERSISTENT ANOVULATION

- Increased BMI
- Elevated testosterone (T) levels and polycystic ovaries (PO)
- **Not predictive** are serum LH levels or IR

# Q1 - US DIAGNOSTIC CRITERIA

In adolescents, what are  
the ultrasonographic  
criteria to diagnose PCO?



# Q1 - US DIAGNOSTIC CRITERIA

- In adolescents with normal cycles 30-40% prevalence of PO in asymptomatic girls.
- No compelling criteria to define PCOM have been established for adolescents (<17 y).

*Witchel et al. The diagnosis of PCOS in adolescences. Clinical practice Committee Publication  
Hormone Research in pediatrics; 2015;83;376-389*

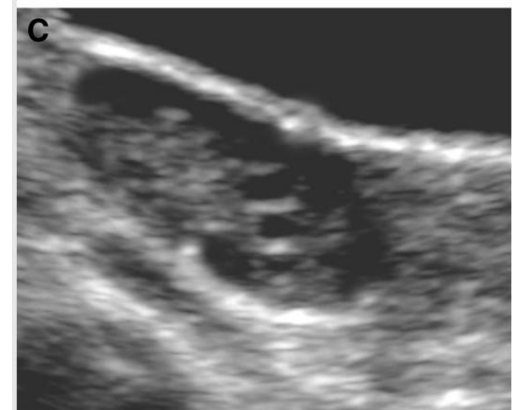
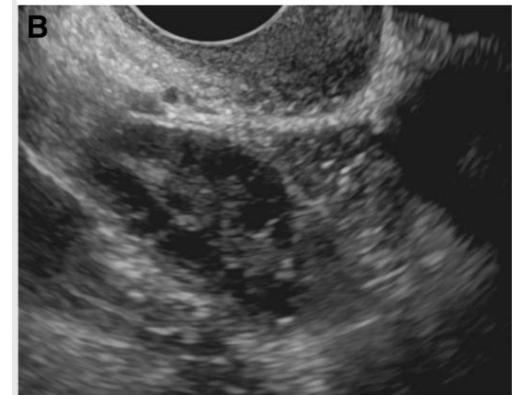
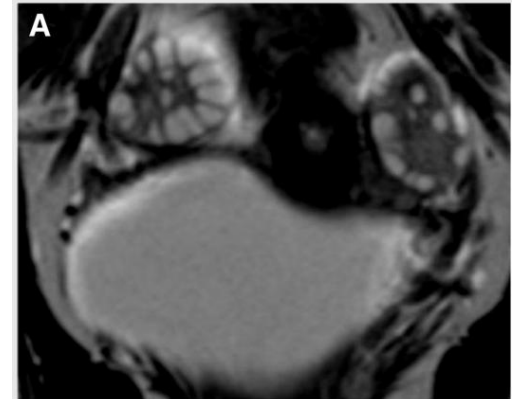
# Q1 - US RECOMMENADATION

- Ovarian volume >12.0 cm (by formula for a prolate ellipsoid) can be considered enlarged.
- Follicle counts should not be utilized to define PCOM in adolescents.
- AMH concentrations should not be used to characterize PCOM

*Assesment and management of PCOS, summary of evidence- based guideline; MJA195(6)2011  
Consensus on women's health aspects of polycystic ovary syndrome (PCOS): ESHRE/ASRM-PCOS  
Consensus Workshop Group BCJM Fauser et al. Fertility & Sterility, Jan2012;97(1):28-38  
Diagnosis and treatment of PCOS: An endocrine society clinical practice guidelines  
J Clin Endocrinol Metab; Dec (2013) 98 (12) 4565  
Witchel et al. The diagnosis of PCOS in adolescences. Clinical practice Committee Publication  
Hormone Research in pediatrics; 2015;83;376-389*

# Clinical utility of magnetic resonance imaging and ultrasonography for diagnosis of polycystic ovary syndrome in adolescent girls

Lisa E. Kenigsberg, M.D.,<sup>a</sup> Chhavi Agarwal, M.D.,<sup>a</sup> Sanghun Sin, M.S.,<sup>b</sup> Keivan Shifteh, M.D.,<sup>c</sup> Carmen R. Isasi, M.D., Ph.D.,<sup>d</sup> Rebecca Crespi, N.P.,<sup>a</sup> Janeta Ivanova,<sup>b</sup> Susan M. Coupey, M.D.,<sup>e</sup> Rubina A. Heptulla, M.D.,<sup>a</sup> and Raanan Arens, M.D.<sup>b</sup>



**Conclusion** US measures smaller OV than **MRI**, cannot **accurately detect follicle** number, and is a poor imaging modality for characterizing PCOs in adolescents with suspected PCOS.

For adolescents in whom diagnosis of PCOS remains uncertain after clinical and laboratory evaluation, MRI should be considered as a diagnostic imaging modality.

*Fertil Steril* 2015;104:1302–9.

## Q1 HYPERANDROGENISM

- Presence of **hyperandrogenemia (adult)**
- Persistent acne, poorly responsive to topical dermatological tt > evaluation
- Moderate to severe hirsutism, or progressive hirsutism during the adolescent years

*Blank SK, et al. Polycystic ovary syndrome in adolescence. Ann NY Acad Sci 2008; 1135:76–84.*

*Witchel et al. The diagnosis of PCOS in adolescences. Clinical practice Committee Publication  
Hormone Research in pediatrics; 2015;83;376-389*

# Q1 DIAGNOSTIC CRITERIA SUMMARY

In adolescents, what are  
the most effective criteria  
to diagnose PCOS ?

# RECOMMENDATIONS FOR DIAGNOSIS

Diagnosis based on a complete picture that includes:

- Clinical signs and symptoms of androgen excess
- Increased androgen levels (Total and/or freeT)
- Persistent Oligomenorrhea > 2-3 years after menarche
- Exclusion of other causes of hyperandrogenemia

**A high index of awareness is needed in order to initiate a thorough medical and laboratory evaluation for signs and symptoms of PCOS , including a f/h of PCOS**

Diagnosis and treatment of PCOS: An endocrine society clinical practice guidelines  
J Clin Endocrinol Metab; Dec (2013) 98 (12) 4565

## Q 2 INVESTIGATION

- Abdominal circumference, BMI
- Androgen profile (Testosterone, SHBG, 17-OH-P)
- $FAI = 100 \times \text{Total Testosterone} / \text{SHBG}$  (0.3 - 5.6)
- FSH, LH, oestradiol and progesterone
- AMH (surrogate marker for US, yet to be proven in adolescents)
- Prolactin/TSH/adrenal or ovarian tumours

*Witchel et al. The diagnosis of PCOS in adolescences. Clinical practice Committee Publication  
Hormone Research in pediatrics; 2015;83;376-389*

## Q 2 INVESTIGATION

- Screening every 3-5 years with OGTT (fasting & 2h 75gr oral G load). HbA1C considered if refusal to do or unable to do test
- Screening for depression and anxiety, and QoL evaluation
- Screening for CVD risk factors (smoking, HTN, dyslipidemia, obesity, obstructive sleep apnea, non-alcoholic fatty liver)

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**Adolescence and polycystic ovary syndrome: current concepts on diagnosis and treatment**P. M. Spritzer,<sup>1</sup> A. B. Motta<sup>2</sup>

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*Int J Clin Pract*, November 2015, 69, 11, 1236–1246. doi: 10.1111/ijcp.12719**Q3 ATTITUDE****Table 1** Main treatment options for adolescents with polycystic ovary syndrome

Treatment	Mechanism of action	Reproductive and Metabolic effects
Weight loss	Increases insulin sensitivity Increases SHBG May decrease ovarian androgen secretion	Improves lipid and glucose profile and blood pressure control May improve/restore regular menses
Insulin sensitizer drugs	Decreases glucose levels and increases insulin action May decrease ovarian androgen secretion	Additional benefits in weight loss as adjuvant for dietary and lifestyle interventions May improve/restore regular menses May induce ovulatory cycles
E+P pills	Decreases GnRH pulses and gonadotropin secretion Decreases ovarian androgen secretion Increases SHBG At long-term may decrease 5- $\alpha$ -reductase activity Decreases non-opposed oestrogen action on endometrium	Reduces hirsutism Decreases total and free circulating androgens Promotes menstrual cyclicity Protect against endometrial hyperplasia
Antiandrogens	Compete with circulating androgens for binding with androgen receptors Decreases 5- $\alpha$ -reductase activity	Decreases acne and hirsutism

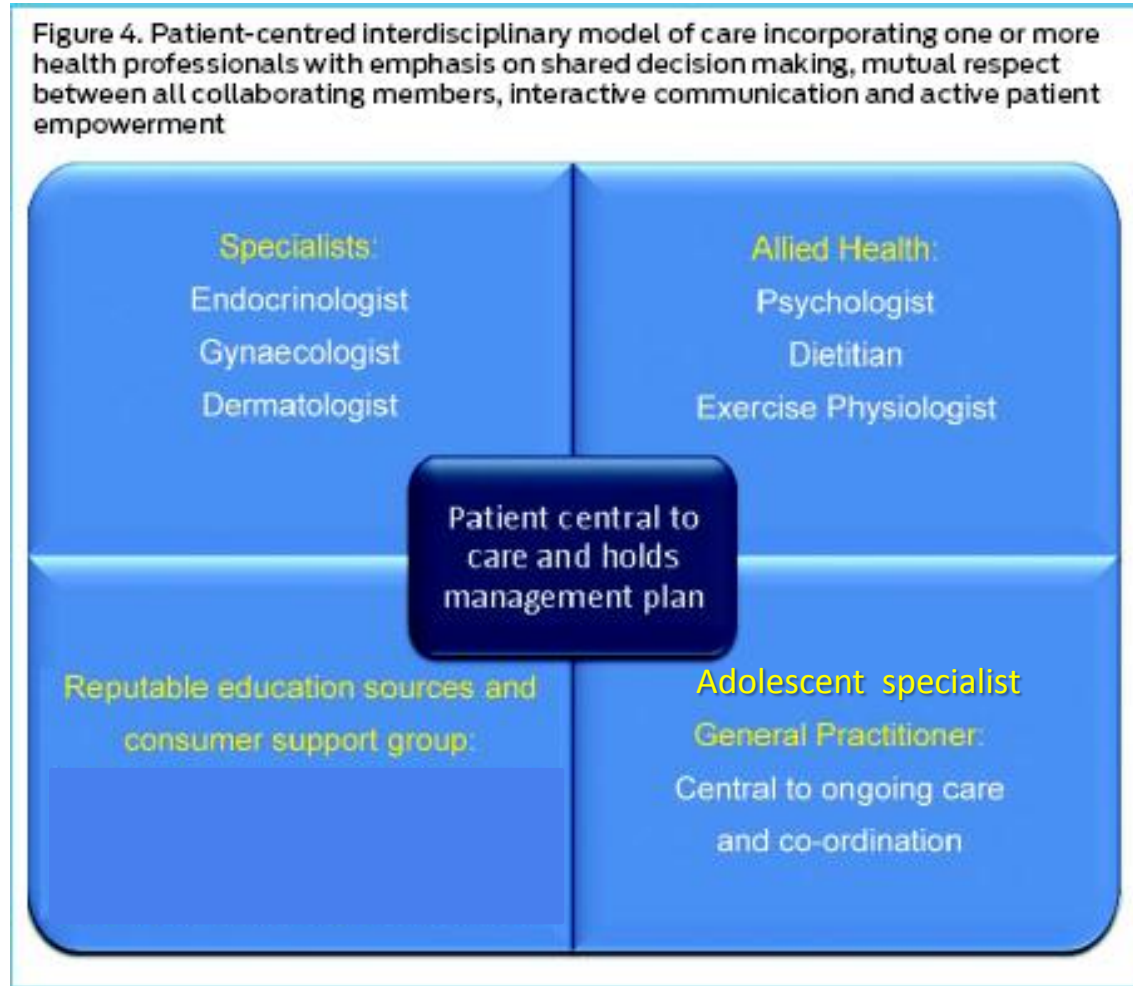
SHBG, sex hormone binding globulin; E+P pills, combined oestrogen plus progestin contraceptive pills; GnRH, gonadotropin-releasing hormone.

# QUALITY OF LIFE

Figure 6. Anxiety and depression, poor body image, eating disorders and psychosexual dysfunction are all likely to affect quality of life in polycystic ovary syndrome



# INTERDISCIPLINARY CARE



# TAKE HOME MESSAGE

- Criteria for the diagnosis of PCOS in adolescents differ from those used for older women.
- Groups at risk (e.g., obese, hirsute, irregular menses) should be identified, but physicians should be cautious of over-diagnosing PCOS
- Individual PCOS manifestations in adolescents (e.g., obesity, hirsutism, irregular menses) should be treated even in the absence of a definite diagnosis.
- Interdisciplinary care is key

## Are Young Adult Women With Polycystic Ovary Syndrome Slipping Through the Healthcare Cracks?

Anuja Dokras and Selma Feldman Witchel

Division of Reproductive Endocrinology, Department of Obstetrics and Gynecology (A.D.), University of Pennsylvania, Philadelphia, Pennsylvania 19104; and Division of Pediatric Endocrinology (S.F.W.), Department of Pediatrics, Children's Hospital of Pittsburgh of University of Pittsburgh Medical Center (UPMC), Pittsburgh, Pennsylvania 15224

Polycystic ovary syndrome (PCOS) is a common endocrine disorder often diagnosed in adolescence or early adulthood. In adolescence, the many similarities between normal features of puberty and symptoms of PCOS make it challenging to confirm the diagnosis. Even among adult women, the changing definitions of PCOS may lead to inaccurate diagnoses. Women may present with a variety of symptoms to different healthcare providers and may be treated only for the presenting symptoms without evaluation of the syndrome and its associated morbidities. Timely evaluations, accurate diagnosis, appropriate interventions, and multidisciplinary healthcare teams can be valuable because women with PCOS have an increased risk for obesity, impaired glucose tolerance, diabetes, dyslipidemia, metabolic syndrome, infertility, endometrial cancer, and anxiety and mood disorders. Appropriate transition of care for the adolescent from pediatric to adult healthcare providers should include education of the patient and her parents regarding the chronic nature of the syndrome and the need for continued follow-up. Girls with symptoms suggestive of PCOS who fail to fulfill diagnostic criteria should undergo prolonged observation. Early identification of PCOS at different entry points in the healthcare system will require physician education and improved access. (J Clin Endocrinol Metab 99: 1583–1585, 2014)

## Are Young Adult Women With Polycystic Ovary Syndrome Slipping Through the Healthcare Cracks?

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Division of Reproductive Endocrinology, Department of Obstetrics and Gynecology (A.D.), University of Pennsylvania, Philadelphia, Pennsylvania 19104; and Division of Pediatric Endocrinology (S.F.W.), Department of Pediatrics, Children's Hospital of Pittsburgh of University of Pittsburgh Medical Center (UPMC), Pittsburgh, Pennsylvania 15224

Polycystic ovary syndrome (PCOS) is a common endocrine disorder often diagnosed in adolescence or early adulthood. In the past, the symptoms of PCOS were often overlooked because of the changing definitions and the expanding list of symptoms to diagnose the condition. However, the features of puberty and early adulthood are now being recognized, and young adult women, they present with a variety of symptoms. Timely evaluations, accurate diagnosis, appropriate interventions, and multidisciplinary healthcare teams can be valuable because women with PCOS have an increased risk for obesity, impaired glucose tolerance, diabetes, dyslipidemia, metabolic syndrome, infertility, endometrial cancer, and anxiety and mood disorders. Appropriate transition of care for the adolescent from pediatric to adult healthcare providers should include education of the patient and her parents regarding the chronic nature of the syndrome and the need for continued follow-up. Girls with symptoms suggestive of PCOS who fail to fulfill diagnostic criteria should undergo prolonged observation. Early identification of PCOS at different entry points in the healthcare system will require physician education and improved access. (*J Clin Endocrinol Metab* 99: 1583–1585, 2014)

NOT ANYMORE

# THANK YOU



**Table 6.** Considerations for Use of Combined HCs, Including Pill, Patch, and Vaginal Ring, in Women with PCOS Based on Relevant Conditions

Criteria	Further Classification	Conditions			
		1	2	3	4
		A condition for which there is no restriction for the use of the contraceptive method	A condition for which the advantages of using the method generally outweigh the theoretical or proven risks	A condition for which the theoretical or proven risks usually outweigh the advantages of using the method	A condition that represents an unacceptable health risk if the contraceptive method is used
Age	Menarche to <40 y	X			
	>40 y		X		
Smoking	Age ≥35 y		X		
	Age ≥35 y and smokes <15 cigarettes/d			X	
	Age ≥35 y and smokes ≥15 cigarettes/d				X
Obesity	BMI <30 kg/m <sup>2</sup>		X		
	BMI ≥30 kg/m <sup>2</sup>		X		
Hypertension	History of gestational hypertension	X			
	Adequately controlled hypertension			X	
	Elevated blood pressure levels (properly taken measurements): systolic, 140–159 mm Hg; or diastolic, 90–99 mm Hg			X	
	Elevated blood pressure levels (properly taken measurements): systolic, ≥160 mm Hg; or diastolic, ≥100 mm Hg				X
Dyslipidemia	Known hyperlipidemias		X	X	
Depression	Depressive disorders	X			
Unexplained vaginal bleeding (suspicious for serious condition)	Before evaluation <sup>a</sup>		X		
Diabetes	History of gestational diabetes		X		
	Nonvascular diabetes, insulin or non-insulin dependent		X		
	Vascular disease including neuropathy, retinopathy, nephropathy <sup>b</sup>			X	X
	Diabetes duration >20 y <sup>b</sup>			X	X

**Diagnosis and treatment of PCOS: An endocrine society clinical practice guidelines**  
**J Clin Endocrinol Metab; Dec (2013) 98 (12) 4565**