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Welcoming....

Our New Patron Members

Dr. Aparna Padgaonkar
Dr. Kavita Mantry
Dr. Madhuri Joshi
Dr. Nirja Chawla
Dr. Shreyas Padgaonkar

Our New Associate Member

Dr. Amina Meer

Our New Life Members

Dr. Amit Tandon
Dr. Arpita Goen
Dr. Janaki Than K.M. Pillai
Dr. Kunjimoideen K.U
Dr. Manju V. K.
Dr. Naina Jaitli

Dr. Padmapriya Paramasivam
Dr. Rachana Jalal
Dr. Rachana Sampathkumar
Dr. Ratnabali Chakravorty
Dr. Remya Menon

Dr. Sandhya Chhasatia
Dr. Sanjukta Sen
Dr. Shashwati Halder Kayal
Dr. Snehaleta Manu Kuris
Dr. Supriya Patil

Dr. Udayan Kundu
Dr. Uma Ram
Dr. Urmila Patil
Dr. Veena M.
Dr. Zohra Mastoor

Total of 6 Modules

Developed with support of Sun Pharma

RECENTLY LAUNCHED MODULES

Excellence in PCOS, Experience in Reproductive Technology

Authors – Dr. Duru Shah & Dr. Madhuri Patil

Module 1 Ovulation Induction in Polycystic Ovary Syndrome
Module 2 Polycystic Ovary Syndrome and Endometriosis
Module 3 Ovarian Aging: Challenges and Therapeutic Options
Module 4 Role of Adjuvants in Infertility Management: from Physiology to Therapeutics
Module 5 Male Infertility
Module 6 Assisted Reproductive Technology

Online content available on the below link
http://www.pcosindia.org/expert-modules.php
Editorial

Dear Friends,

"PANDORA" the Newsletter, of the PCOS Society of India reaches out to 40,000 physicians globally, and is dedicated to giving you the news from our Society and also some scientific updates.

The PCOS Society of India is a Collective of various disciplines of medicine ie. gynaecology, endocrinology, dermatology, medicine etc. which deal with PCOS. We also have Associate Members who are not physicians but are Nutritionists, physiotherapists, etc. who manage the issues related to PCOS.

Our Website is loaded with educational material which currently is open to all, but very soon we will be restricting access to the educational content, to only members of the Society. To become a Member or Patron of the Society, please download the form from the website http://www.pcosindia.org/membership.php and join us in our endeavour to manage our PCOS patients better.

We have started the year 2019 with many academic activities, some of which we reported in our last issue, January-April 2019. In this issue we bring to you what has elapsed between our last report to you and our future scheduled events. Our Webinar Series with Monash University have been extremely successful with very meaningful practical discussions. I urge you to check our schedule for further sessions, and if you have missed any of them, you could still see them archived on our website in the “Education Section” http://www.pcosindia.org. I thank the USV team for making it possible for us to disseminate this brilliant academic initiative to promote the latest International Recommendations on the management of PCOS.

The Course on “Art of ART in PCOS” which is a 6 day hands-on course for PCOS and Assisted Reproduction, was held between March 18th-23rd, 2019. It was house full with 16 candidates which is all we accept at a time. Please read the details on page 5, and register for the next course in September 2019. I am extremely thankful to our esteemed faculty and to the Torrent team and Origio for supporting our endeavour which is targeted towards upcoming Gynaecologists.

We have completed 2 of our CME’s in collaboration with the “Endocrine Dept. of KEM Hospital” which focused on the Endocrine aspects of PCOS. We thank the USV team for assisting us in organizing these extremely interactive CME’s, of which we have 2 more to go.

We now look forward to our Annual Conference between 23rd to 25th August, 2019, being organized in Mumbai, by our Vice President Dr. Shashank Joshi jointly with Dr. Piya Ballani Thakkar, both Endocrinologists.

Do block your dates and you will hear from us soon.

Also block your dates 1st, 2nd, 3rd November, 2019 for an exciting full day Masterclass on “PCOS in Puberty and Adolescence” in collaboration with the International Gynaecological and Endocrine Society (ISGE) with 4 excellent international speakers, followed by a day of solving clinical dilemmas with experts. Please block your dates, you will soon get all details.

The immediate next event which will run from May-October 2019 will be a Series of 6 Webinars of 2 hours each on “Infertility Management in PCOS” dedicated to post graduate students and clinicians interested in infertility management.

The webinar will cover 6 topics, with each topic devoted to the current evidence, the new research and the clinical experience of experts on the various aspects of infertility in PCOS. We thank the Torrent team in assisting us in reaching out globally through the digital platform. Please read further details on page 11.

The educational content on Infertility and Assisted Reproduction has been compressed into 6 brilliant Modules entitled “EXPERT” (Experiences in PCOS evidence in Reproductive Technology) which have been supported by Sun Pharma and hard copies delivered to about 3000 gynecologists! The digital version of these are available on the PCOS Society website http://www.pcosindia.org/expert-modules.php. The Modules have been developed by Dr. Madhuri Patil and myself and I thank Madhuri for all her support. Please read on page 2 for further details.

I offer my sincere gratitude to our authors who have contributed 2 brilliant articles in this issue of Pandora, which are always the star attractions of Pandora. Please read their articles on pages 6 & 9.

We look forward to you enjoying this 10th issue of PANDORA and looking forward to wonderful academic year.

Wishing you all the best

Warm regards,

Duru Shah
Founder President,
The PCOS Society
CME on “Endocrine Aspects of PCOS” – 3rd Feb 2019, Mumbai

An Interactive CME on "Endocrine Aspects of PCOS" organized by PCOS Society of India in collaboration with Endocrine Department KEM Hospital and The Thane Obstetric Gynaecology Society (TOGS) was held on the 3rd of February 2019, in Thane. It was supported by USV Pharma.

The CME was dedicated to the endocrinological aspects of PCOS, which is a multi factorial complex disorder, requiring multi faculty approach due to its diverse manifestations, which requires strategic treatment and management were tackled with abundant knowledge and evidence based management guidelines.

Dr. Madhuri Patil, a fertility specialist, who came from Bengaluru, represented the PCOS SOCIETY, gave an exhaustive overview on the diagnosis and investigations of PCOS.

Dr. Lila, an endocrinologist emphasized on the rationale for Metformin treatment, clarifying all doubts.

Dr. Swarupa Iyer, a gynaecologist from Thane spoke on menstrual disorders and infertility.

Dr. Nalini Shah, an endocrinologist from Mumbai gave an extremely informative and lucid presentation on case based approach in ruling out secondary causes of PCOS and Hyperandrogenism.

The Panel discussion moderated by Dr. Rajnish Patel, President of TOGS on the Endocrine perspective of PCOS was well conducted and well received withpractical tips on The Management of Obesity, hypothyroidism and hyperprolactinemia.

The Panelists were Endocrinologists from KEM Hospital, Mumbai, Dr. Tushar, Dr. Swati, Dr. Lila, Dr. Nalini Shah and Gynaecologists from Thane, Dr. Alaka Godbole, Dr. Uma Bansal and Dr. Sandhya Saharan.

It was an extremely interactive panel with enthusiastic audience participation and a touch of humour when it came to management of obesity, which made the atmosphere more lively and interesting.

The CME proved to be one to remember for years to come.

The USV Team did a great job in both organizing and coordinating with TOGS to ensure there was a grand venue with great food and overwhelming attendance by local delegates, numbering 182.

CME on "Adolescent PCOS" – 30th March 2019, Bangalore

The PCOS Society (India) held a half day CME on "Adolescent PCOS", on 30th March 2019 at Bangalore. This was in collaboration with the Bangalore Obstetric and Gynaecological Society and saw a participation of experts from varied disciplines like Gynecology, Endocrinology, Cosmetology, Bariatric surgery, Nutrition and Psychology. As it was a multidisciplinary CME it involved discussion on all aspects of adolescent PCOS, from diagnosis to management. Each speaker put forth the different aspects of adolescent PCOS extremely successfully. The session was attended by 160 delegates with an extremely well attended interactive session. All doubts were clarified on the subject of adolescent PCOS, making the delegates very satisfied.

This CME was supported by an unconditional educational grant from Bayer Zydus Pharma, which was truly appreciated.
The first hands-on 6 day Certificate course on The Art of ART in PCOS was conducted from the 18th of March to the 23rd of March 2019. The course mainly focused on PCOS Women and had didactic lectures, case discussions and demonstration of sperm preparation techniques, IVF and ICSI procedures with freezing of sperms, oocytes and embryos. The candidates had the opportunity to improve their oocyte retrieval and embryo transfer skills on the Simulators. The course also focused on the medicolegal aspects of ART including third party reproduction, PCPNBDT and Adoption. Course content was provided in the form of Six Modules on various aspects of ART, several E-books and guidelines. The number of candidates was limited to sixteen, hence all the lectures were very interactive, and all queries were resolved.

We had an excellent faculty including fertility specialists Drs Padma Rekha Jirge, Shreyas Padgaonkar, Sujata Kar, Pratap Kumar, Ameet Patki, Kanthi Bansal, Parikshit Tank; embryologists Rajvi Mehta and Kersi Avari and Medico legal expert Hitesh Bhatt. The entire faculties for the course were stalwarts in the field of ART. All the candidates have been offered a complimentary observational week at any of the ART centers approved by the PCOS society (India).

The feedback from all the candidates was very good as all of them thought they would be able to improvise on their present practice of managing infertile PCOS patients.

The next course has been scheduled on 16th September to the 21st of September 2019. Registration can be completed by direct online payment on the PCOS Society website or by sending your cheque or Demand Draft to the PCOS Society office or through net banking.

Feedback from the ART Course delegates

"One of the finest ART Course I have attended"

"Very informative Sessions"

"The hardwork, dedication and knowledge of the teachers have inspired me to excel and work hard. Would like to attend further courses."

"Excellent workshop! Very Practical"

ART Centres for Observership

<table>
<thead>
<tr>
<th>Faculty, Email id</th>
<th>Centers &amp; Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Kanthi Bansal, <a href="mailto:kanthibansal@gmail.com">kanthibansal@gmail.com</a></td>
<td>Allahabad 24th April to 27th April</td>
</tr>
<tr>
<td>Varanasi 28th April to 2nd May Ahmedabad 6th May to 10th May</td>
<td></td>
</tr>
<tr>
<td>Dr. Kersi Avari, <a href="mailto:kersiavari@hotmail.com">kersiavari@hotmail.com</a></td>
<td>Mumbai 6th-10th May</td>
</tr>
<tr>
<td>Dr. Duru Shah, <a href="mailto:durushah@gmail.com">durushah@gmail.com</a></td>
<td>Mumbai Gynaecworld, Dates to be confirmed as per mutual convenience.</td>
</tr>
<tr>
<td>Dr. Madhuri Patil, <a href="mailto:drmadhuripatil59@gmail.com">drmadhuripatil59@gmail.com</a></td>
<td>Bangalore, Dates to be confirmed as per mutual convenience.</td>
</tr>
<tr>
<td>Dr. Sujata Kar, <a href="mailto:suju63@yahoo.com">suju63@yahoo.com</a></td>
<td>KCHPL, Bhubaneswar – based on the candidates requirements</td>
</tr>
<tr>
<td>Dr. Rekha Jirge, <a href="mailto:rekha.jirge@gmail.com">rekha.jirge@gmail.com</a></td>
<td>Kolhapur</td>
</tr>
</tbody>
</table>

A Hands-on 6 days Certificate Course on The Art of ART in PCOS

Dates: Course 2 – 16th to 21st Sept. 2019

Venue: Origio India Private Limited – A Cooper Surgical Company C-401, Delphi, Hiranandani Business Park, Powai, Mumbai 400 076

Course material will be provided

Observational Week in an IVF Centre

Register on www.pcosindia.org
Introduction
We have led the development of the first international evidence-based guideline for the diagnosis and management of polycystic ovary syndrome (PCOS), with an integrated translation program incorporating health professional and consumer resources. The development process involved an extensive Australian-led international and multidisciplinary collaboration of health professionals and consumers over two years. The guideline aims to support both health professionals and women with PCOS in improving care, health outcomes and quality of life.

Context and background
Polycystic ovary syndrome (PCOS) is a significant public health issue with reproductive, metabolic and psychological features. PCOS is one of the most common conditions in reproductive aged women affecting 8–13% of reproductive-aged women1-4 with up to 70% of affected women remaining undiagnosed1. Presentation varies by ethnicity and in high-risk populations, prevalence and complications are higher5-7. Women with PCOS present with diverse features including psychological (anxiety, depression, body image)8-10, reproductive (irregular menstrual cycles, hirsutism, infertility and pregnancy complications)11 and metabolic features (insulin resistance (IR), metabolic syndrome, prediabetes, type 2 diabetes (DM2) and cardiovascular risk factors).12-13

Diagnosis and treatment of PCOS remain controversial with challenges defining individual components within the diagnostic criteria, significant clinical heterogeneity generating a range of phenotypes with or without obesity, ethnic differences and variation in clinical features across the life course. These factors contribute to variation in diagnosis and care across geographical regions and health professional groups.13 This culminates in delayed diagnosis, poor diagnosis experience and dissatisfaction with care reported by women internationally.13 These challenges are exacerbated by a lack of recognition of the diverse features of PCOS, inadequate funding for quality research and a lack of comprehensive international evidence-based guidelines.14 In this context, there was a compelling need for development and translation of an international evidence-based guideline for assessment and management of PCOS, addressing psychological, metabolic and reproductive features of PCOS, promoting consistent evidence-based care and guiding and encouraging research in PCOS.

The extensive international guideline network across our partners and collaborators engaged in prioritization of clinical questions and information needs, identification of gaps in knowledge and care and into translation preferences and information needs for health professionals and consumers. This stakeholder engagement directly informed the guideline and translation program and involved over 3000 health professionals and consumers with PCOS. Our partners and collaborators contributed members to the guideline governance, development and translation committees and formed special interest groups with considerable expertise in PCOS to provide feedback during the public consultation process and are engaged in translation and evaluation.

Governance
Governance included international representation across the Advisory Committee, Project Board, Consumer Reference Group, Translation Committee and five multidisciplinary Guideline Development Groups comprising partner and collaborator nominated experts, practicing clinicians and consumers. Guideline development groups and special interest groups/experts were nominated by the partner and collaborator organizations. The Australian Centre for Research Excellence in PCOS (CREPCOS), funded by the National Health and Medical Research Council (NHMRC), led and primarily funded the guideline development. In this endeavour, we partnered with the European Society of Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM). Thirty five other societies partnered in the development of the guideline including the PCOS Society of India with Dr.Duru Shah involved as an expert guideline developer.

Methods
Guideline development engagement and processes were extensive and followed best practice. Four project board and 15 guideline development group face to face meetings occurred across Europe, USA and Australia over 15 months. Sixty prioritized clinical questions were addressed with 40 systematic and 20 narrative reviews, generating 166 recommendations and practice points.

Recommendations were formulated using the considered judgement process in the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework15 across the quality of available evidence, integrating clinical expertise and consumer preference, and considering the applicability, feasibility, equity, cost effectiveness, implementation and value for consumers and health professionals through the GRADE framework. Implementation issues and international health systems and settings were also considered.

Community and consumer engagement
Extensive engagement and formative research on unmet needs of women with PCOS was a key driver for this work. Far-reaching engagement included focus groups and then surveys of over 1500 women with PCOS. We adopted the International Association for Public Participation (IAPA), Public Participation Spectrum framework, in which consumer’s capacity to participate was built and enhanced throughout the process. Consumers were engaged in all phases as active contributors within a distributed decision making environment, ensuring that the lived experiences of women with PCOS were prioritized. Consumer representatives were informed about the process of participation and at GDG meetings were present to embed consumer perspectives within the GRADE decision-making process. Consumers were empowered to ensure that all decisions optimised participation in care. Consumer organizations proactively participated in feedback and public consultation processes and have co-designed and will continue to guide and influence the implementation, translation and dissemination program.

Guideline recommendations
Recommendations and practice points cover the following broad areas: diagnosis, screening and risk assessment depending on life stage; emotional well being; healthy lifestyle; pharmacological treatment for non-fertility indications; and assessment and treatment of infertility.

Summary of clinical changes in the recommendations
- Endorsement of the Rotterdam PCOS diagnostic criteria in adults (two of clinical or biochemical hyperandrogenism, ovulatory dysfunction, or polycystic ovaries on ultrasound).
- Where irregular menstrual cycles and hyperandrogenism are present, ultrasound not necessary in diagnosis.
- In adolescents and those within 8 years of menarche, both hyperandrogenism and ovulatory dysfunction are required, with ultrasound not recommended, as it over-laps with the normal physiology around puberty.
- The definition of irregular cycles is more clearly defined based on gynaecological age.
- Androgens to be measured in diagnosis, although the definition of irregular cycles is more clearly defined based on gynaecological age.
- Interventions for non-fertility indications; and assessment and treatment of infertility.
- The definition of irregular cycles is more clearly defined based on gynaecological age.
- Androgens to be measured in diagnosis are specified along with optimal assays.
- Ultrasound criteria are specified across a range of age and settings.
- Anti-mullerian hormone levels, although not used in the definition of irregular cycles, will continue to be measured.
- The definition of irregular cycles is more clearly defined based on gynaecological age.
- Androgens to be measured in diagnosis are specified along with optimal assays.
- Ultrasound criteria are specified across a range of age and settings.
- Anti-mullerian hormone levels, although not used in the definition of irregular cycles, will continue to be measured.

Continued on page 8
### Webinar on International PCOS Guidelines

**Brings to you a series of 12 FREE Webinars based on the latest International PCOS Guidelines**

**One Webinar every 15 days for 1 hr duration**

**Dates**
Feb. to Aug. 2019

**A unique opportunity to solve your queries by the experts who helped in creating the Guidelines**

<table>
<thead>
<tr>
<th>Month</th>
<th>Date</th>
<th>Topic</th>
<th>Speaker</th>
<th>Timings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb</td>
<td>12th Feb., Tuesday</td>
<td>Are women with PCOS at a higher risk of cardiovascular disease? How should we screen and monitor CV risk?</td>
<td>Dr. Kurt Barnhart</td>
<td>7:30 pm Indian Standard Time</td>
</tr>
<tr>
<td>March</td>
<td>28th March, Thursday</td>
<td>How should we diagnose PCOS? Is it different for adolescents?</td>
<td>Dr. Kathy Hoeger</td>
<td>7:30 pm Indian Standard Time</td>
</tr>
<tr>
<td>April</td>
<td>11th April, Thursday</td>
<td>Does PCOS impact fertility?</td>
<td>Dr. Michael Costello</td>
<td>2 pm Indian Standard Time</td>
</tr>
<tr>
<td>May</td>
<td>16th May, Thursday</td>
<td>What are the principles of drug therapy in PCOS? What should we prescribe and when?</td>
<td>Dr. Helena Teede</td>
<td>2 pm Indian Standard Time</td>
</tr>
<tr>
<td></td>
<td>28th May, Tuesday</td>
<td>What contributes to weight gain in PCOS women? Is it her genes, her altered metabolic function, her psychological morbidity, obesogenic environment or her lifestyle?</td>
<td>Dr. Anuja Dokras</td>
<td>7:30 pm Indian Standard Time</td>
</tr>
<tr>
<td>June</td>
<td>13th June, Thursday</td>
<td>What exactly do we mean by Lifestyle modifications* in PCOS? Do they really help?</td>
<td>Dr. Rob Norman</td>
<td>2-4 pm Indian Standard Time</td>
</tr>
<tr>
<td></td>
<td>25th June, Tuesday</td>
<td>What is insulin resistance, why does it occur and how should it be managed?</td>
<td>Dr. Elisabet Stener-Victorin</td>
<td>7:30 pm Indian Standard Time</td>
</tr>
<tr>
<td>July</td>
<td>11th July, Thursday</td>
<td>Use of Gonadotropins in Infertility Management in PCOS Women</td>
<td>Dr. Clare Boothryd</td>
<td>To be announced</td>
</tr>
<tr>
<td></td>
<td>30th July, Tuesday</td>
<td>What should we expect during pregnancy in PCOS? Any precautions before, during and after pregnancy?</td>
<td>Dr. Roger Hart</td>
<td>2 pm Indian Standard Time</td>
</tr>
<tr>
<td>August</td>
<td>12th Aug, Monday</td>
<td>Hyperandrogenism in PCOS</td>
<td>Dr. Joop Laven</td>
<td>2 pm Indian Standard Time</td>
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<tr>
<td></td>
<td>29th Aug., Thursday</td>
<td>To be announced</td>
<td></td>
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</tbody>
</table>
Metformin recommended in addition or alone, primarily for metabolic features 

Letrozole, where permitted by national bodies, is first-line pharmacological infertility therapy with, clomiphene and metformin having a role alone and in combination. 

Gonadotrophins and laparoscopic surgery are second line and in vitro fertilization third line in isolated PCOS. 

Guideline translation 

A comprehensive, international translation program is disseminating, translating and amplifying the impact of the guideline. Central to the translation and dissemination program is active engagement of 37 international partners and collaborator organizations and leading health experts, across 71 countries, who are leveraging their extensive reach and influence to promote guideline uptake. Leading consumer groups internationally and translation organizations are strongly engaged and committed to translation and impact. 

The guiding principles of the comprehensive international translation and dissemination program are: 

- components are informed by the needs and preferences of women with PCOS; 
- resources are co-created with, and attuned to, the needs of end-users; and 
- dissemination strategies are multi-faceted, multi-modal and refined to the communication channels of end-users. 

The research translation program uses a multi-model approach delivering individual, community and system level impact. It targets a range of stakeholders including; consumers and their significant others and those who serve consumers such as specialist physicians (endocrinologists, obstetricians and gynaecologists, fertility specialists) primary care practitioners, allied health professionals (dietitians, exercise physiologists, psychologists) public health professionals, nurses, midwives and policy makers. 

The aims of the program are: 

- To guide implementation of the guideline recommendations. 
- To build the capability of health professionals to deliver high-quality, consistent, evidence-based assessment and management of PCOS. 
- To augment the health literacy of PCOS health consumers, leading to early diagnosis and improved health outcomes; 
- To promote best-practice PCOS models of care . 
- To influence health policy towards an evidence-based approach. 

Reach 

1. Consumers 

Over 1,70,000 consumers have been directly reached via a range of modalities such as; web-based platforms, national media coverage (TV, radio, conventional media and digital platforms), collaborating organization reach and App based platforms such as AskPCOS. A range of strategies were employed to reach PCOS consumers. The primary dissemination strategy of the translation program was to engage with consumer representative organizations and associations both in Australia and internationally (Appendix 1: Collaborating organizations). All consumer focused translation resources were co-created with consumers. In addition, the comprehensive media campaign achieved national coverage with an estimated number of exposures per consumer of up to three across mainstream and digital platforms. 

2. Health professionals 

Up to 40,000 health professionals were directly reached in presentations and up to 800,000 indirectly. A range of modalities were used such as; an international conference program, high-impact journals, health media (conventional media, web-based and social media) with deep penetration achieved within collaborating societies. Multidisciplinary health professionals (endocrinologists, obstetricians and gynaecologists, exercise physiologists, nurses, psychologists, fertility specialists and dietitians) from 37 societies across 7 continents that formed an international collaboration to develop the PCOS guideline and sign up to participate in the translation program. Health professionals were consulted on knowledge and clinical gaps 4 and had input into the research questions informing the rigorous evidence-synthesis undertaken. Health professionals also formed part of the five guideline-development groups (GDGs) with active input into the consensus process informing the guideline recommendations. All practice tools and decision-making support tools were co-created with health professionals. In addition, the comprehensive media campaign with the health media sector had extensive reach and penetration. 

Impact 

The guideline and translation program impact the following areas: 

- Cost reduction to the health system. 
- Improved patient satisfaction. 
- Early diagnosis rates increased. 
- Increased feasibility of implementation. 
- Increased health professional capacity to deliver evidence-based care. 
- Consistency in the assessment and management of PCOS. 
- Increased consumer awareness and PCOS related health literacy. 
- Guidance to health professional on interdisciplinary care. 
- Uptake and implementation of best practice models of care. 
- Policy outcomes supporting evidence-based care. 
- Feasibility and clinical care improvements will have significant impacts on reducing costs and improving the patient experience and on health outcomes. 

Outputs 

The following translation outputs were informed by extensive consultation with end-users: 

- co-designed digital booklets catering to low and medium health literacy levels 
- a consumer booklet co-designed with and for Aboriginal and Torres Strait Islander women 
- an internationally accessible, accredited health professional learning module hosted on the UK based Futurelearn platform 
- an innovative, consumer PCOS App (AskPCOS) providing comprehensive evidence-based PCOS health information, a self-diagnostic function, a Question Prompt List (QPL) to optimize health practitioner engagement and a commonly asked questions list. 

We would like to acknowledge and thank Professor Duru Shah for her expert guidance and participation in the Centre for Research Excellence in PCOS International Advisory Panel. We also thank the PCOS Society India, one of the international collaborating partners in this guideline. Additionally, The Society is actively participating in the dissemination of the guideline through the delivery of a series of webinars. The webinars will feature leading members within the PCOS guideline development groups and focus on a range of topics of interest to health professionals. The aim of the webinars is to increase the capacity of health practitioners within India to deliver evidence-based PCOS care. 

The full guideline, including 166 recommendations and practice points can be downloaded at https://www.monash.edu/medicine/sphpm/mchr/pocos/guideline 

References 


International evidence-based guideline for the assessment and management of PCOS 2018 

Continued from page 6
Estrogens or female sex hormones are important for sexual and reproductive development in women. It’s primary source are the ovaries but it is also produced by fat cells and the adrenals. The term "estrogen" refers to all of the chemically similar hormones in this group, which are estrone, estradiol and estriol.

Estrogen as a hormone has different roles to play in each aspect of a woman’s life. It is evident in the unique pubertal development and reproductive development. Natural menopause is defined as the permanent cessation of menstrual periods, determined retrospectively after a woman has experienced 12 months of amenorrhea without any other obvious pathological or physiological cause. It occurs at a median age of 51.4 years in normal women and is a reflection of complete, or near complete, ovarian follicular depletion, with resulting hypoestrogenemia and high follicle-stimulating hormone (FSH) concentrations.

The hypoestrogenic state of menopause may lead to various symptoms such as depression, vaginal dryness and subsequent atrophy, sexual dysfunction, mastalgia, migraines. The long term consequences of estrogen deficiency include bone loss, loss of collagen in the skin, higher risk of CVD, dementia and a possibility of it acting as a contributing factor to the development of osteoarthritis. In the early postmenopausal years, women who do not take estrogen therapy typically gain fat mass and lose lean mass. Some, but not all, studies, suggest that postmenopausal hormone therapy is associated with a decrease in central fat distribution.

Menopause and HRT

The reasoning behind the use of HRT as a preventative treatment for menopausal women was based on the evidence for its protective effect on the cardiovascular system as well as wide range of studies dating back to the 1960s showing estrogen deficiency may have a causal role in postmenopausal osteoporosis. The mechanism whereby estradiol-(E2) prevented osteoporosis was shown to involve augmenting osteoblast survival and decreasing pro-osteoclastic signals.

In 2002 Writing Group for the Women’s Health Initiative (WHI)published a multicenter double-blind, placebo-controlled trial which was initiated to assess the effect of HRT on decreasing cardiovascular events in women between ages of 50-79 yrs. The outcome of the study was widely publicized because the results of one arm of the trial where the women were given E+P, showed that there was a significant overall increase in the risk of CVD,breast cancer, stroke and dementia. In the other arm of the trial where more than 10,000 women were only given 0.625 of conjugated estradiol, there was found to be an increased risk of stroke similar to E+P increased dementia, but no change in risk of coronary vascular diseases and an overall decrease in the incidence of hip and vertebral fractures. These outcomes were backed by another ‘Million women retrospective cohort study’ where 1,804,100 women between ages of 50-64 were recruited to assess the association between specific types of HRT and risk of breast cancer. The outcomes suggested increased risk with increased duration of HRT;10 years of use led to 19 cases per 1000 users of combination HRT. These two studies made the world of HRT stop in its heels as 65% women on HRT stopped treatment. But 2 yrs later, 1 in 4 women restarted HRT. Does the formulation of estrogen make a difference in clinical use?

Synthetic conjugated Estradiol (Ethinyl Estradiol)

Most potent
Most commonly used in oral contraception

Animal derived (Conjugated equine estrogen)

Mostly estronesulphate and 10 minor components

Plant derived

17 β Estradiol – micronized
Estradiol valerate – better absorbed

Estradiol valerate

Is a natural estrogen and is found to be safer than the synthetic counterparts. It contains the most active estrogen i.e. 17 β estradiol. It is available in the micronized form and is convenient for oral administration. It has increased dissolusion and bioavailability when taken orally as esterification prevents extensive first pass metabolism in liver and GI tract. It is safe even for long-term use (adherence is good even after 7 yrs. of therapy).

When compared to other forms of estrogen such as ethinyl estradiol, there has been no significant effect on the breast density, blood pressure, lipid profile. Doses as low as 17 β estradiol 0.25 mgms, appear to be effective for vasomotor symptoms and to prevent bone loss.

### Estradiol valerate vs other conjugated estrogens

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Estradiol valerate</th>
<th>Conjugated estrogen (CE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasomotor symptoms</td>
<td>Hot flushes, severe throbs, and breast tenderness is lower</td>
<td>Presence of vasomotor symptoms are higher with CE</td>
</tr>
<tr>
<td>Lipid profile and cardio-protective effect</td>
<td>Offers favorable lipid profile</td>
<td>Lesser favorable lipid profile</td>
</tr>
<tr>
<td>Endothelial function</td>
<td>EV improves endothelial function and reduces plasma levels of endothelin</td>
<td>Vasoprotective effect not reported</td>
</tr>
<tr>
<td>Plasma homocysteine level</td>
<td>EV has no effect on plasma homocysteine level</td>
<td>Effect on homocysteine level not reported</td>
</tr>
</tbody>
</table>

Only E or P as well?

Endometrial hyperplasia and cancer can occur after as little as six months of unopposed estrogen therapy; as a result, a progestin should be added in women who have not had a hysterectomy. Women who have undergone hysterectomy should not receive a progestin.

Route of administration

Once a decision has been made to treat a woman with menopausal hormone therapy (MHT), consideration should be given not only to the type of estrogen but also to the the route by which it is to be given. The route of administration is significant as transdermal estrogen is as effective as oral estrogen for preserving bone density and is associated with a lower risk of venous thrombosis and stroke, and it has less of an effect on serum lipid concentrations when compared with a comparable dose of oral estrogen. Women being treated for menopausal symptoms such as hot flashes require systemic estrogen. Vaginal estrogen is most commonly used in very low doses for the management of vaginal atrophy. Higher doses of vaginal estrogen can be used to treat vasomotor symptoms, much like any of the preparations for systemic use.

Current recommendations for HRT

**American heart association**

- HRT should not be initiated for the sole purpose of primary prevention of CVD
- HRT should not be initiated for the purpose of secondary prevention
- HRT should not be initiated within one year of a cardiac event even for other indication, since increased risk from HRT is seen in the first year a pro inflammatory state
- If there is a CVD event or immobilization for a women on HRT – it should be MHT is the most appropriate therapy for fracture prevention in the early menopause. [A]
- Oral estrogen therapy is contraindicated in women with personal history of VTE. [A]
- Transdermal estrogen therapy should be the first choice in obese women suffering from climacteric symptoms. [B]
MHT should not be used to enhance cognitive function. [A] Estrogen therapy may be of short-term cognitive benefit to surgically menopausal women when initiated at the time of oophorectomy. [B] The increased risk of breast cancer is primarily associated with the addition of a synthetic progestogen to estrogen therapy (CEE + MPA continuous combined therapy) and related to the duration of use. [B] The risk may be lower with micronized progesterone or dydrogesterone than with a synthetic progestogen. [C]

Based on the evidence to date, the association between MHT use and ovarian cancer remains unclear. MHT use may be associated with a reduced risk of gastric cancer. [C]

When Vulvo-vaginal atrophy is the sole symptom, local estrogen treatment should be the first choice. [B]

FDA approved indications for HRT

- Vasomotor symptoms
- Prevention of bone loss
- Hypo estrogenism – primary hypo-hypo / POI / Postsurgical
- Genito urinary syndrome of menopause

Absolute contraindications for HRT

- Breast cancer
- Previous venous thromboembolism
- Active liver disease
- Coronary heart disease
- Stroke

Conclusion

The benefits of HRT outweigh the risks for the treatment of menopausal symptoms if prescribed before the age 60 or within 10 years after menopause. HRT potentially prevents osteoporosis-related fractures in at-risk women before the age of 60 or within 10 years after menopause.

HRT using standard-dose monotherapy with estrogen may decrease CHD and all-cause mortality in women younger than 60 years and within 10 years of menopause.

Oral HRT increases the risk for VTE and ischemic stroke, but the absolute risk is rare in women younger than 60 years

Increased risk for breast cancer may be a concern with combination HRT (E + P) and may be related to duration of use. The risk is small and after treatment is discontinued.
Quiz

I. How does L-carnitine have an impact on male infertility?
   a. Leads to adenosine triphosphate depletion.
   b. Epididymal maturation of spermatozoa.
   c. Acts as a donor of acetyl group facilitating transfer of fatty acid from mitochondria to cytosol.
   d. All of the above.
   
II. Source of L-carnitine:
   a. Red meat
   b. Legumes
   c. Lysine methylation in kidney and liver
   d. A & C
   e. B & C

III. How does L-carnitine improve the reproductive functions?
   a. Free radical scavenging.
   b. Increases the action of capases 3, 7, 8.
   c. Increases the cytokines like TNF-α, INF-β, IL-6 and IL-2.
   d. All of the above.

IV. L-carnitine has proven to be beneficial for some PCOS women by:
   a. Lowering the blood glucose levels and improving insulin sensitivity.
   b. Helps in weight loss.
   c. Increases the response to ovarian stimulation.
   d. All of the above.

V. Highest concentration of myoinositol is found in:
   a. Beans.
   b. Corns.
   c. Nuts.
   d. All of the above.

VI. What is the MI/DCI ratio in follicular fluid of normal and PCOS women respectively?
   a. 1 : 1 / 1 : 50.
   b. 100:1 / 0.2 : 1.
   c. 0.2 : 1 : 100.
   d. 1 : 50 / 0.2 : 1.

VII. How does L-carnitine help in male fertility?
   a. Epididymal maturation of spermatozoa.
   b. Energy for sperm respiration and motility.
   c. Increases the viability of sperm.
   d. All the above.

VIII. Action of myoinositol in PCOS women:
   a. Dichiroinositol decreases the insulin sensitivity.
   b. Improves FSH signalling
   c. Oocyte maturation
   d. All of the above.
   e. None of the above

IX. Better action of myoinositol is seen after ------- weeks of treatment.
   a. 8
   b. 6
   c. 12
   d. Immediately

X. Clinical studies have shown that both myo-inositol and D-chiro-inositol may also:
   a. Have no effect on serum androgens (male hormones)
   b. Decrease triglycerides
   c. Increase HDL cholesterol (the good cholesterol)
   d. Lower systolic and diastolic blood pressure

XI. Myoinositol has been used in the treatment of:
   a. Panic disorder and depression
   b. Diabetic neuropathy
   c. PCOS (polycystic ovarian syndrome)
   d. Alzheimer’s disease
   e. All of the above

Quiz Answers

I. d
II. e
III. d
IV. d
V. d
VI. a
VII. d
VIII. e
IX. d
X. b
XI. d
From Preconception Pregnancy to Lactation

Shelcal-XT

Calcium Carbonate 500 mg, Vitamin D3 200 IU, Riboflavin 5 mg.
L-lysine hydrochloride 100 mg, Calcium Pantothenate 20 mg.
The High Potency Calcium with Extraordinary Power of Vitamin D3 & Active Form of Vitamin B.

In PCOS Patients,

L-Carnitine in the Purest Form

CARNISURE-500

L-Carnitine 500 mg Tablets

The Metabolic Energizer

Coming Soon...

Shelcal-XT MOM

powered by

Torrent Pharma

In Obese PCOS patients with BMI>29*

NORMÖZ DS

MI 1.1 gm, DCI:27.6 mg, Chromium Picolinate & Vitamin D3, tab

Double Strength for Effective Action in Obese PCOS

Study of 128 obese PCOS patients with high dose MI+DCI (1g MI+25mg DCI) twice a day vs Metformin 1500 mg every day for 3 months confirms...

DS

Significantly better results in...

Weight reduction
Resumption of spontaneous ovulation
Spontaneous pregnancy