

A Comprehensive Review On: Polycystic Ovarian Disease and It's Impact on Health Care of Female

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ABSTRACT

Poly cystic ovarian disease (PCOD) is a complex pathophysiology and common endocrine, metabolic disorder that affect the ovaries and can lead to physiological, irregular menstrual cycle also the main reason of infertility and also formation of cysts in the ovary. It's also know as Polycystic ovarian syndrome. PCOS is a hormonal condition that results in larger ovaries with little cysts around the periphery. This hormonal disorder globally affect the more then 5 - 15% ladies at their puberty age leading to decreasing the level of Oestrogen and Progesterone. They also have increasing the level of Androgen. This ovulation process stimulated by bodily hormone. The clear root of PCOS it's genetic alliance and hormonal disbalance with most usual manifestation , acne on face, hirsutism, insulin resistance, hair loss, obesity. The acumen regarding management of PCOD through healthy life style with physical activity like Yoga. PCOS is considered focus on implement or modification in way of living style to the community (education, stop smoking, rational diet , not consumption of alcohol and weight management) when necessary are of the importance and early obstruction to fend off future morbidities.

Keywords: PCOD, Androgen, Hirsutism, insulin resistance, morbidities

1. INTRODUCTION

Poly cystic ovarian disease is a endocrine , hormonal complex disorder that transpire the reproductive age of women world wide which following as a consequence of irregular menstrual cycle. This complication occur the teen age. PCOS has not till proper treatment the ovaries develop numerous tiny fluid- filled sacs called “ follicles” which contain immature eggs, often appearing as cyst on imaging along the outer edge of the ovaries , due to immature follicles , women with PCOS often experience irregular or absent ovulation , leading to difficulties with fertility. The size of cyst is varies to every women. (25, 22, 44) Types of cyst consist into the ovaries is hemorrhagic cyst, endometriotic cyst, chocolate cyst, multifollicular ovaries, endometriosis cyst. Prevalence estimated to be anywhere between 5-15% . Multifactorial diseases involve excess production of androgen which is male sex hormones which cause functional ovarian Hyperandrogenism which is prohibited the ovulation. (28) Additionally, it has been shown that 5% of lean women and 28% of unselected obese women have PCOS. Using US statistics and historically lower prevalence estimates, the menstrual disruption accounted for 31%, infertility⁽¹⁴⁾ for 12%, and POOS-associated diabetes for 40% of the estimated \$400 million economic burden of PCOS in Australia, indicating a significant financial and health impact. Promisingly, nutritional, behavioral, and exercise-based lifestyle interventions increase fertility and dramatically lower newborn costs. (14,26,23)

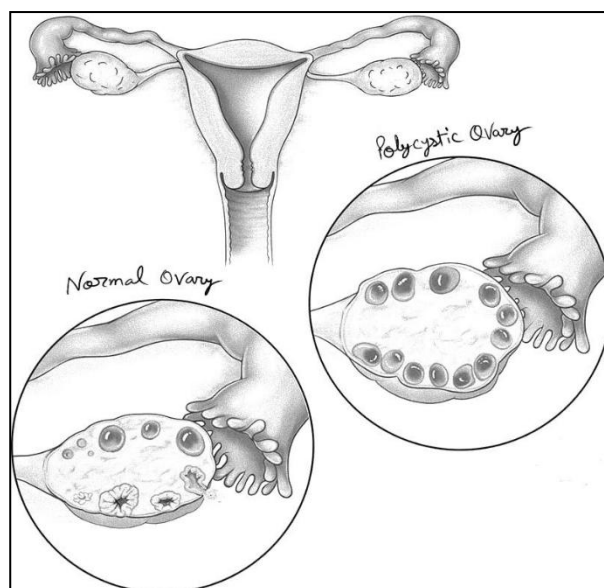


Figure 1. Poly cystic ovarian disease

Epidemiology of PCOD

According to (WHO) World health organization , affects an estimated 8 - 13% of reproductive aged women by Polycystics ovary syndrome , up to 70% of affected women be still un-diagnosed world wide.⁽³⁷⁾ Numerous chronic health conditions that impact both physical and mental well-being are linked to PCOD.⁽²²⁾ In India its varies depending on the communitical studies and the selection of diagnostic criteria. The Rifeness of PCOD in India ranges from 3.7% to 22.5%. A 2022 study found that the weighted national prevalence of PCOD was 7.2% using the National institute of Health 1990 criteria.⁽¹⁵⁾ Abnormalities in the leptinadiponectin , oxidative stress and auto immune disorder are varies the mechanism studied regarding pathogenesis of PCOD. According to Pharmacovigilance with PCOD involve initiating a systematic approach to monitor and report any adverse event associated with the drugs using in the treatment of PCOD. In the International classification of Diseases (ICD) , PCOD (Polycystic Ovary Disease) is classified under the category of endocrine, nutritional and metabolic diseases.^(1,2)

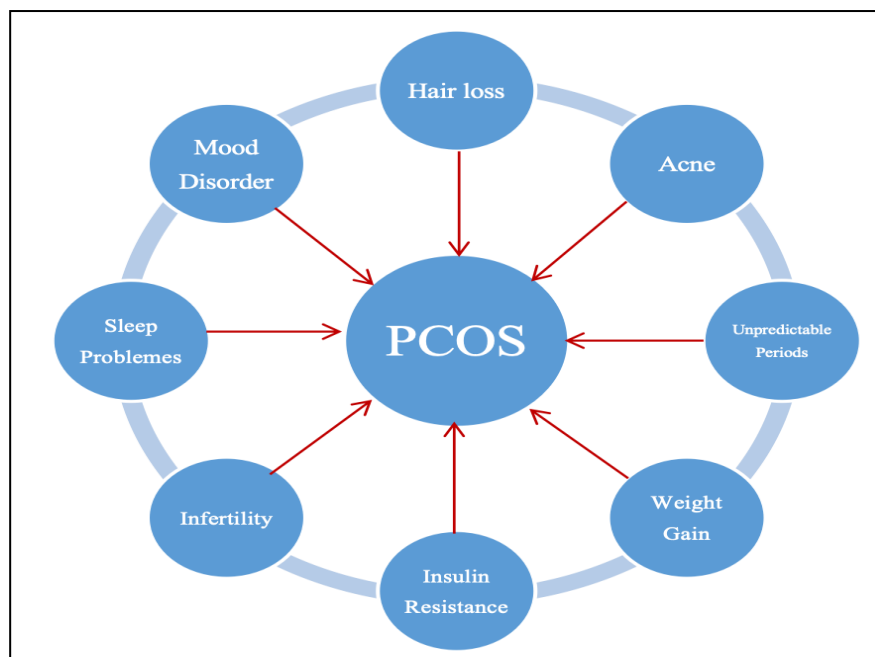
History of PCOD

American Gynaecologist F. Stein, Sr. and Michael L. Leventhal initially reported the illness in 1935 and it was from that it's "Stein Leventhal syndrome". Both Gynaecologist attended Rush medical college, bron in Chicago, and worked at Michael Reese Hospital their whole careers. According to these two researchers, seven women four of whom were obese presented with bilateral enlarged polycystic ovaries with thickened tunica, amenorrhoea, hirsutism and ovulation problem. Following bilateral ovarian wedge surgery, which involved removing one half to three quarters of each ovary, all seven returned to having regular menstrual cycle and two of them became pregnant also. A total of 75 women who also had wedge resection were later reported by Stein; 65% of them became pregnant and 90% of them reported having regular menstrual flow. After noticing a return of menstrual flow in multiple amenorrhoeic patients after ovarian biopsy, Stein and Leventhal devised the wedge resection technique. They hypothesised that follicles were unable to access and escape from the ovary's surface because of the thicker ovarian capsule.^(22,36)

Pathophysiology

Despite being one of the most common endocrinopathies, the exact cause is still unknown. The variability of PCOS may represent multiple pathophysiological causes, despite the fact that the description of each contributing pathophysiological mechanism has been sluggish to emerge.

It has historically been helpful to think of polycystic ovarian syndrome as the outcome of a "vicious cycle," which might start at any one of numerous entry sites.⁽⁴²⁾ PCOD is a common , complex, metabolically and reproductive disorder distinguished by high level of Androgen in women the age of 25 - 45. It's strongly influence by several factor - such as disturbance of the hypothalamic pituitary ovarian axis, hyperinsulinemia and hyper androgenism which menifesets as hirsutismm ,acne. Disease is associated with the thinning of endometrium wall of the ovaries . Neuroendocrine disruption is characterized by increasing frequency of gonadotropin releasing hormone and reduced negative feedback frame sex steroids in hypothalamus.^(22,20)

PCOD Affect the Body**Figure 2. PCOD affect the body**

The accurate pathophysiology of PCOD is still unclear and complex. Despite the fact that the detailed discussion beyond this review, the hormonal imbalance is shown to be caused by the combination of increasing androgen or insulin underpinning of PCOD. Heredity or Environment contributes to imbalance in hormone with the combination of other factors, which include obesity, problem in ovulation, ovarian cancer and hypothalamic-pituitary abnormalities to contribute to the reason of the PCOD. However, the lack of a reliable way to evaluate insulin resistance or hyperandrogenism has made it challenging to determine the pathophysiology of PCOD. It shows approx 70% to 80% of cases in women which is due to Hyperandrogenism as PCOD etiology. According to National Institute of Health (NIH) criteria, those women who are overweight are diagnosed as PCOS around 60% to 80% is contributed pathophysiological condition of Insulin Resistance.^(20,22,23) Hyperandrogenism in PCOS is probably caused by a variety of factors, abnormalities of the GnRH release pulse frequency [increased release of luteinizing hormone (LH)] as well as elevated adrenal P450c17 activity. The ovary and glands most likely have a role in PCOS's elevated androgen production.⁽³⁴⁾

Adipocytes are essential for metabolic and reproductive activities because they release adipocytokines. Insulin sensitivity, lipolysis, dyslipidemia, and aberrant fat accumulation in visceral organs are all signs of PCOS adipocyte dysfunction. It has been determined that the adipocytes of women with PCOS secrete different amounts of signaling molecules, including resistin, visfatin, retinol-binding protein-4, leptin, and adiponectin. An adipokine called leptin regulates metabolism and communicates to the central nervous system the state of feeding. Although leptin levels seem to be higher in PCOS-afflicted women, research is still ongoing to determine exactly how it affects the hypothalamic-pituitary-ovarian axis. On the other hand, PCOS causes a drop in adiponectin.^(20,22,42)

Etiology of PCOD

- The reason behind the PCOD is the consuming the heavy, unhealthy or rich meal in the diet, inculcating the quality or quantity of food consuming as well as water.
- Unhealthy and imbalance of the life style.
- There are some factors in presence of stressful environment of the working female.
- Imbalance of hormone due to stressful condition.
- Facing conceiving attributed to PCOS.⁽²¹⁾
- Increase Prolactin level which produces the milk formation into the breast in small age of female.
- Alcohol consuming and smoking also associated with the PCOD.
- Increase level of androgen, testosterone lead to PCOD.
- Using contraceptive pill, self abortion and excessive take of self medication is the main reason of menstruation cycle.

irregular^(17,18)

- Excessive use of home remedies also responsible for the the PCOD.

Risk Associated

Genetic factor- Family history is a risk factor of PCOS. Mono-zygotic twins (identical twins) if one twin has PCOS is highly likely to also have PCOS to another twins as well, that indicating genetic competent. First degree relative with PCOS is regard as a heritable condition because of the way that instances tend to cluster in family. The mode of inheritance is still unknown the challenge of acquiring sufficiently high sample size to enable sufficient statistical power are some of the problem impeding advancement in the field.^(7,8)

A numerous studies shown that , risk factor for hypertension is more common multiple chronic condition . Endothelial dysfunction as seen elevated endothelin level and elevated aldosterone concentration linked to insulin resistance , are potential cause of hypertension in PCOS. ^(22,20)

Obesity- Obesity and excessive weight gain are chronic disease condition world .Its is also a responsible for the PCOD like infertility, hyper-androgenism, hirsutism, complication in gestation periods both independently and by exacerbating , kindly advice given to maintain the weight.^(4,6)

Metabolic disorders - PCOS is associated with meta metabolic disorders such as insulin resistance is further responsible for the risk of Type 2 Diabetes, enhanced impaired tolerance of glucose and cardio vascular disease as well.⁽⁴⁸⁾ Pre- pubertal, early onset menarche. Large or small for gestational age. It could be relaed to androgen exposure.^(21,22)

Environmental pollutant- Environmental pollutant and toxins such as tobacco, smoke. These volitant have property to produce adverse effect in the organism and absorb through the skin and mucous membrane or inhaled property.⁽⁴⁵⁾ Various studies shown that those women working in the industry, such as Lead industry associated with injurious chemical like Heavy metal causing Arsenic, Mercury, Lead poisoning affect the human health as well as reproduction and characterized by various disease. ^(21,22)

Unhealthy diet and life style- Urban and Rural life style also associated with health. sudden change of curriculum of the daily routine of the female.⁽²⁵⁾

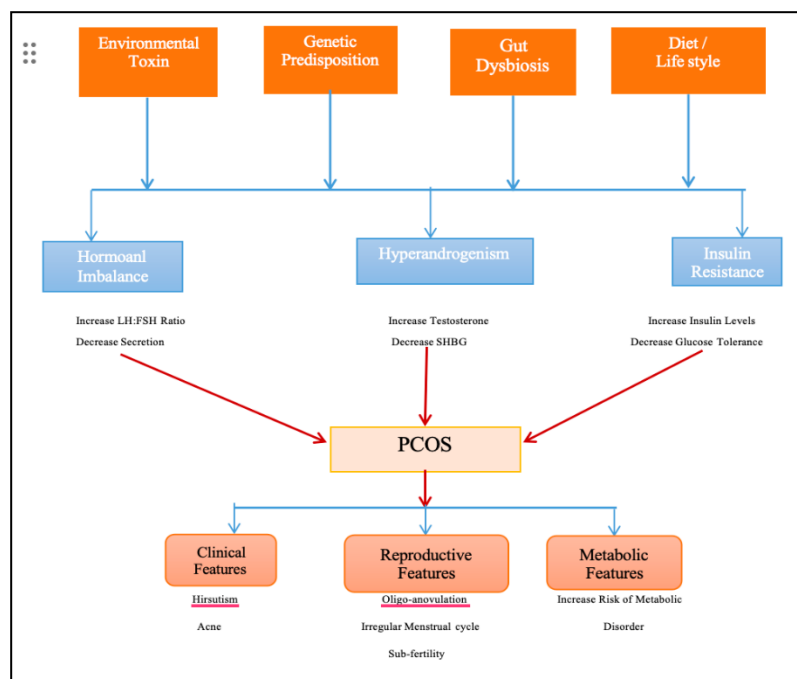


Figure 3. Risk associated

Stress - Stress can worsen the symptoms of poly cystic ovary syndrome and may even be a primary cause.⁽⁴⁹⁾ Stress can increase the level of cortisol, the body's stress hormone, which can lead to higher testosterone levels and worsen PCOS symptoms.⁽²⁵⁾

Sleep disturbance - Sleep disturbance for often analogous with poly cystic ovary syndrome and can impact the condition in several ways like irregular mensuration cycle , insulin resistance, weight gain, cardiovascular risk, etc.⁽⁴³⁾

Gut microbiota - Gut microbiota bile acid interleukin 22 axis play a role in development of PCOS.⁽²²⁾

Neuroendocrine dysregulation - PCOS involve dysregulation of the Hypothalamus -Pituitary ovarian axis, which can lead to hyper secretion of luteinizing hormone.^(47,48)

Clinical features

The clinical presentation of PCOD is differ universally. Women with PCOS facing problem with clinical manifestation of hyperandrogenism, Menstrual irregularity , infertility (Chronic an ovulation). Oligomenorrhea, amenorrhoea and prolong erratic menstrual bleeding in commonly observed in disbalancement in menstrual cycle with PCOS. However the 30% women have their normal menses. Approximately compared to 30% to 40% of women with amenorrhea 85% to 90% of women with oligomenorrhoea also have PCOD. Patients with PCOS have many 8 mm sized cysts in their ovarian sac. The ovary conatain more than 12 cysts.⁽¹³⁾ This disorder cause infertility in about 70% of females.⁽³¹⁾ Some other clinical features associative with the overweight (obesity) and resistance of insulin , (NAFLD) Non alcoholic fatty liver disease which is metabolic syndrome.⁽⁹⁾ Women with PCOS may facing the difficulties in ovulation , have high level of androgen or have various small cyst present on the ovaries which lead to the infertility. The Reproductive abnormalities included menstrual dysfunction, Gonadotropin dynamics, Endometrial cancer risk showing ovarian abnormalities - Ultrasound appearance, follicular development, serum AMH, anovulatory infertility, pregnancy complication. Clinical and biochemical manifestation hyperandrogenism caused Alopecia, hirsutism , Acne vulgaris with PCOS. Associated commodities - coronary heart disease , C- reactive protine , endothelial function and imaging studies, impaired glucose tolerance and type 2 Diabetes, Endometrial cancer, 20% of women frequently have Obstructive sleep Apnea. Some physiological issue - Mood disorder combine with depression and anxiety are prevalent, eating disorder, over all quality of life as well.^(32,18,38,35)

Diagnostic Criteria

The PCOS diagnosis is predicated on the fluctuating existence of three different components:

oligoanovulation, excess of androgen, ultrasound evaluation of ovarian morphology and either bio-chemical or clinical. There is no one diagnostic test that can definitively identify PCOS.⁽¹⁵⁾ The Rotterdam criteria, which call for the presence of two of the three diagnostic criteria in order to diagnose adult women, were approved by the International Evidence-Based Guideline.⁽³³⁾ It is advised to rule out non classic congenital adrenal hyperplasia, hyperprolactinemia (prolactin), and thyroid illness (thyroid stimulating hormone, TSH). In individuals who exhibit amenorrhoea and other unusual characteristics, additional assessment is advised. Hypogonadotropic hypogonadism or Cushing syndrome may be evaluated, and in cases where the androgenic picture is more severe, androgen-producing tumors may be evaluated.⁽²⁰⁾

- UPT Beta HCG - Pregnancy
- Meds - Androgenic steroids, dopamine antagonist
- TSH - Thyroid disease
- Prolactin - Hyperprolactinemia
- FSH/ LH/ E2 - Hypogonadotropic hypogonadism^(26,23)

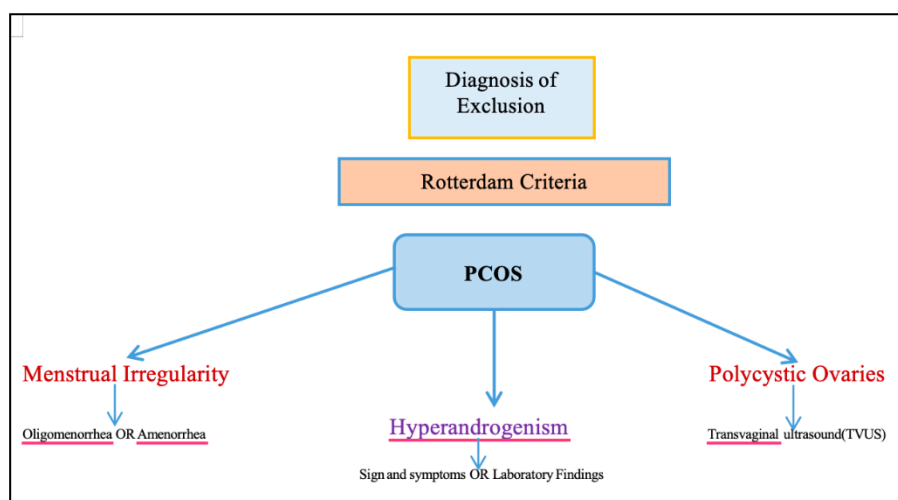


Figure 4. Diagnostic Criteria

Exclude disorder that mimic PCOS -

It has long been recommended that before a PCOS diagnosis is made, prolactin excess, enzymatic steroidogenic abnormalities, and thyroid diseases must be ruled out.

- Pregnancy
- Medication
- Thyroid disease
- Hyperprolactinaemia
- Non-classic congenital adrenal hyperplasia (NCCAH)
- Virilizing tumors, Androgens producing tumors
- Out flow tract obstruction (amenorrhea)
- Cushing syndrome
- Acromegaly

Laboratory Test

- Level of Serum androgen
- Luteinizing hormone OR Follicle stimulating hormone ratio on the third day of mensuration cycle
- Biochemical, screening and lipid profile on fasting.
- Individuals risk factor
- Ultra-sonography
- Medical history
- Such other condition like hypothyroidism, congenital adrenal hyperplasia
- Check insulin level
- Trans vaginal ultrasound
- Pelvic examination⁽³⁴⁾

TREATMENT

A variety of phenotype and clinical manifestation of female with poly cystic ovarian syndrome (PCOS) may help direct therapeutic options for ovulation induction and metabolic protection. Presently Medication treatments include the insulin use sensitizing agents, estrogen synthesis inhibitors, and anti-androgen in along with the birth control pill, or occasionally, the use in surgery of laparoscopic, even though the symptoms may be alleviated by simply implementing lifestyle changes, such as losing weight.⁽⁴⁸⁾ Restoring regular mensuration cycle, reducing insulin secretion, increasing insulin sensitivity, addressing lipid abnormalities, lowering increased testosterone level and treating risk factors like cardiovascular disease, sub clinical inflammation and dyslipidaemia. Lowering activity of PAI-1, and decreasing first-trimester miscarriage are all promising outcomes of metformin therapy in youth to short-term trials. Options for ovulation induction are the main focus of treatment for infertility in patients with PCOS.^(4,7,8) However, an evidence-based study found that many obese and insulin-resistant women with PCOS can induce ovulation with weight loss, exercise, and metformin, which is advised as the first line of treatment. Adolescents, should prioritize lifestyle modifications for the primary prevention of metabolic consequences including heart disease and diabetes mellitus.^(16,18) These measures may prove to be more effective than pharmaceutical therapy. Restoring self-esteem and ensuring good health in adulthood depend on early detection and treatment of PCOS in teenagers.⁽⁴⁸⁾ Adolescent daughters of PCOS moms who get lifestyle therapies that prevent increasing adiposity may also be less likely to develop several metabolic abnormalities associated with PCOS as adults.^(15,26)

Table 1. Management for PCOD

On the Basis of Ayurvedic Perspective	<ul style="list-style-type: none"> ● The cause of all illnesses affecting the uterus and its operation is "mithyaachar." Inappropriate food and activities (including exercise, sleep, and travel) is indicated by mithyaachar. ● Pradusht artava called as ovarian hormones.⁽³⁵⁾ ● Chromosomal and genetic abnormalities is refer as
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	<p>Bijidosha.⁽²⁸⁾</p> <ul style="list-style-type: none"> ● Idiopathic or unknown cause knows as Daiva. ● Aama Chikitsa ● Tridosha⁽³⁷⁾ ● Sodhana ● Samana⁽³⁶⁾
On the basis of Unani Perspective	<p>The condition has not been classified as PCOS in the Unani medical system. Unani doctors under the categories of Hippocrates believed that humoral impairment was the primary cause of the illness (Akhlat).</p> <p>The dominance of Khilte balgham, which raises the viscosity, is the cause of Ehtebase Tams. According to Sina and Majusi, obesity and sue mizaj barid of rehm are two factors that contribute to ehtebase tams. In this group, the Unani doctors listed a number of illnesses, including uqr, ehtebase tams, and qillate tams.⁽³⁷⁾</p> <p>On other treatment like - Body, mass management, diet and exercise Body, mass management, diet and exercise, Lifestyle treatment , Bariatric surgery.⁽³⁸⁾</p> <p>Drugs like Satawar (<i>Asparagus racemosus</i>), Giloe (<i>Tinospora Cordifolia</i>), Triphla, Saunf (<i>Foeniculum vulgare</i>)⁽³⁷⁾</p>
On the basis of Allopathic Perspective	<ul style="list-style-type: none"> ● Clomiphene citrate ● Insulin sensitizer ● Anastrozole and letrozole⁽⁸⁾ ● Glucocorticoids ● metformin⁽³⁷⁾
On the basis of Homeopathy Perspective	<p>For irregular periods , acne, amenorrhea , leucorrhea , back pain can treats with Pulsatilla.</p> <p>Hormones regulation, ovarian cysts, late periods and infertility associated with Sepia. Calcarea Carb Heavy periods with pain ,Controls weight gain can regulate with Calcarea carb.⁽⁵²⁾</p> <p>Natrum Mur , Hepar Sulph, Oleum Jecoris also used for manages hair fall, headaches, pimples, growth of facial hair.</p> <p>For endometriosis in painful periods can use Cimicifuga and Xanthoxylum.⁽⁵³⁾</p>

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