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## SIGNS AND SYMPTOMS

### HEAD

- Dandruff
- Male pattern baldness
- Depression

### FACE

- Excessive hair growth
- Coarse hair growth
- Masculine features

### SKIN

- Dark patches
- Cystic acne

### ABDOMEN

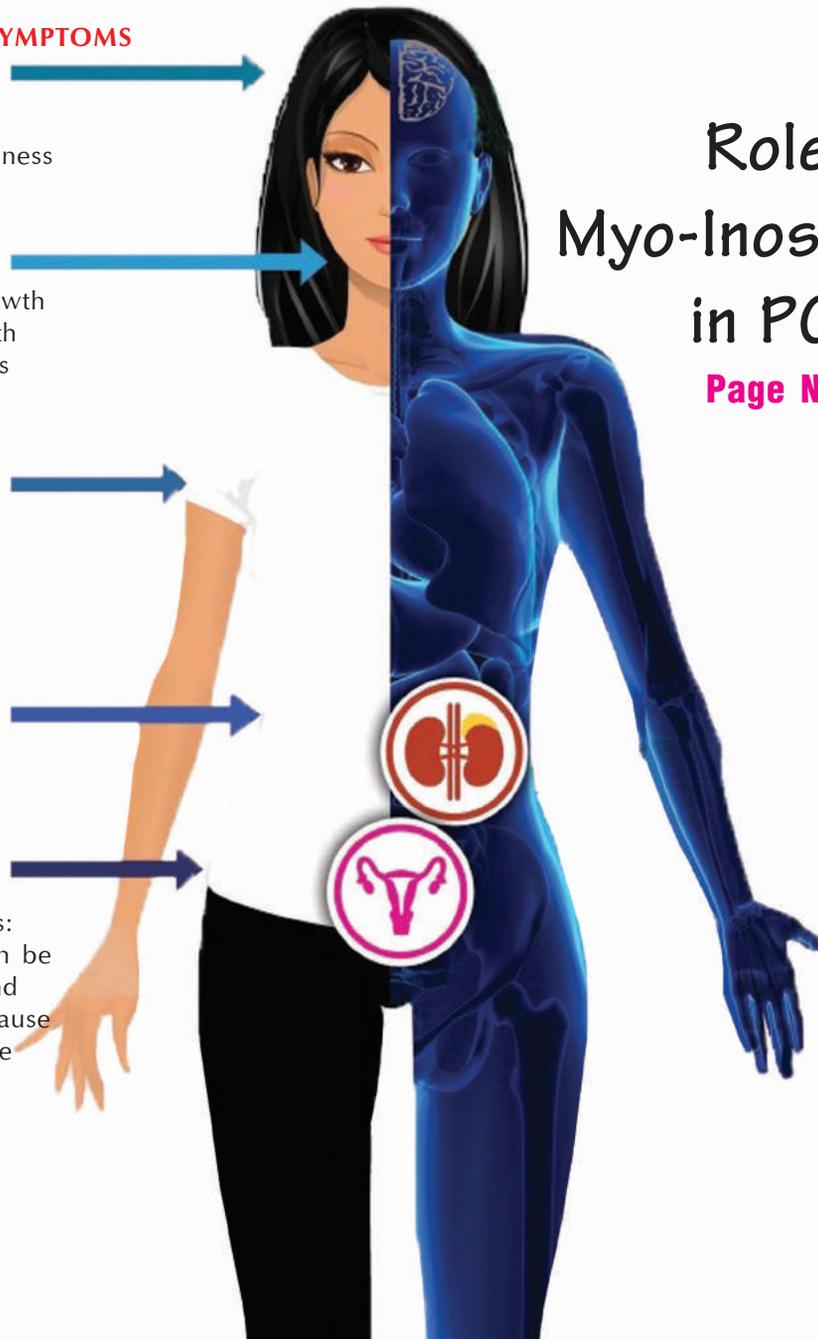
- Weight gain

### PELVIS

- Thickening of wall of uterus
- Polycystic Ovaries: Multiple Cysts can be seen on ultrasound of ovaries, may cause pelvic pain if large enough.
- Irregular menses
- Infertility

## Role of Myo-Inositol (MI) in PCOS

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# Role of Myo-Inositol (MI) in PCOS

**SANJAY AGRAWAL**

## Introduction

Polycystic ovary syndrome (PCOS) is a multifactorial syndrome affecting 10% of women of reproductive age. Since 1980, PCOS is known to be associated with insulin resistance (IR). This has led to extensive investigation on the relationship between insulin and gonadal function<sup>1</sup>. Insulin is synergistic with luteinizing hormone (LH) and enhances the androgen production from theca cells<sup>2</sup> and it also reduces circulating levels of sex hormone binding globulin (SHBG), causing increase of free testosterone. PCOS is a syndrome having both metabolic as well as reproductive morbidities. IR affects 50-80% of the patients with PCOS regardless of BMI<sup>3</sup>.

Evidences show that deficiency of inositol a second messenger of the insulin signaling, may be linked to insulin resistance<sup>4</sup>. Now a day's Inositol is considered the best therapeutic option for PCOS patients. Inositol is a polyalcohol existing as nine different stereo isomers, two of which are insulin mediators: myo-inositol (MI) and D-chiro-inositol (DCI). The studies showed that only MI is present in the follicular fluid and in a direct comparison of MI and DCI only MI was able to improve oocyte and embryo quality. Therefore, Could we say "bye-bye D-chiro-Inositol" in the practice of clinical gynecology and reproductive medicine?

## MYO and DCI: Secondary Messengers

Inositol is considered a member of the B-vitamins and a component of cell membrane. Inositol is available in fruits, beans, grains, and nuts and is also made in the body. MYO and DCI are separate isomers that work differently in the body. MYO and DCI work as these secondary messengers and are thought to be deficient in women suffering from PCOS.

### Which inositol is right for me?

Currently, many studies are being done in direct comparison between MI and DCI in order to elucidate their effects on oocyte quality. Only MI, rather than DCI, was able to improve oocyte and embryo quality<sup>5</sup>. It also states that the DCI to MI ratio was itself insulin dependent. Besides the common features, both inositols have specific action. DCI is mainly responsible for glycogen synthesis; high DCI levels were identified only in glycogen storage tissues<sup>6</sup>. On the other hand, MI plays an important role at ovarian level. Recently, a study has reported that high concentrations of MI positively correlate with high quality and mature oocytes<sup>7</sup>. Furthermore, MI supplementation during IVF protocols has been shown to improve oocyte quality and reduce the number of IU of FSH necessary for ovarian stimulation.

It is important and interesting to note that each tissue has its own MI/DCI ratio and the relative amount of each inositol in a certain tissue reflects inositol(s) specific functions. High DCI levels (always lower than MI) are seen only in glycogen storage tissues

(fat, liver and muscle), while low levels of DCI are seen in tissues that have high glucose utilization, since they need to "have a high energy status" (brain and heart)<sup>8</sup>. Recently a new study stated that one of the causes of poor oocyte quality in PCOS women may be due to the reduced energy metabolism. Literature data have shown that in PCOS women, genes involved in the glucose uptake pathway are down regulated at ovarian level. This data are similar with the findings of a comparative study (MI vs. DCI) stated that only MI has an action at ovarian level, as MI is responsible of glucose cell uptake, improves ovary energy status and hence, it is able to improve oocyte quality. In vivo, DCI is synthesized by an epimerase that converts MI into DCI and, depending on the need of the two different molecules, each tissue has its own conversion rate. Unlike tissues like muscle and liver, ovary never becomes insulin resistant. Therefore, it states that PCOS patients with hyperinsulinemia mostly present with an enhanced MI to DCI epimerization rate in the ovary which results in an increased DCI/MI ratio leading to overproduction of DCI and in MI deficiency. This decrease in MI can be responsible for the poor oocyte quality seen in patients with PCOS<sup>9</sup>. The effects of MI supplementation will improve ovarian response to FSH; and since MI is responsible for glucose cell intake, energy status will also be restored. On the other hand, increasing DCI dosage progressively negatively influences oocyte and embryo quality. Oocyte quality is the main factor influencing the chance of

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a pregnancy; indeed, poor oocyte quality is a cause of infertility as well as an important obstacle for a successful in vitro fertilization (IVF).

Based on these data, Unfer et al developed a theory that created a “DCI paradox”<sup>9</sup>. It suggests that ovaries in PCOS patients are likely to present an increased MI to DCI epimerization which leads to a MI tissue depletion which could eventually lead to poor oocyte quality characteristic of these patients. A combination of both MCI and DCI is only beneficial to people who are completely unable to convert myo-inositol to D-chiro-inositol. Other people who constitute the majority make the conversion, with fullest or with less than optimal efficiency, may definitely going to be benefited from large doses of myo-inositol.

**Conclusion**

Based on the above data and studies MCI is thought to be deficient or in less ratio in oocytes of PCOS patients which may be

leading to decrease in quality of oocyte and infertility? Based on all of these observations, and if the “DCI paradox”, hopefully we could say “byebye D-chiro-Inositol” in the practice of clinical gynecology and reproductive medicine?

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<p>The increased prevalence of thyroid diseases noted in patients suffering from RA has been well established. The association and the probability for existing a common etiology for both the disease have not been fully understood, however some literature studies have shown that they share some common genes, such as CD40, CTLA4, HLA gene complex, and PTPN22, which may increase the risk of disease development. The risk for developing hypothyroidism is higher in patients receiving treatment for RA.</p> <p style="text-align: center;"><b>Journal of The Association of Physicians of India</b></p>	<p>Among the major groups of rickettsioses, commonly reported diseases in India are scrub typhus, murine flea-borne typhus, Indian tick typhus and Q fever. Scrub typhus is the commonest occurring rickettsial infection in India. It is caused by <i>Orientia tsutsugamushi</i>. Scrub typhus is endemic in a part of the world known as the Tsutsugamushi triangle (after the name <i>O. tsutsugamushi</i>). This extends from northern Japan and eastern Russia in the north, to the regions around the Solomon Sea in Pacific Ocean into northern Australia in the south, and to Pakistan and Afghanistan in the west.</p> <p style="text-align: center;"><b>Journal of The Association of Physicians of India</b></p>
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