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*Data on File

1. Joseph A et al. ACS Omega. 2022;7(15):12835–12845. PMID:35474815.

Good Clinical Practice Recommendations (GCPR): Expert Opinion Development Group

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Good Clinical Practice Recommendations (GCPR) for Managing Infertility in Indian Women with Poor Ovarian Response: ISAR Expert Opinion

Introduction & Methodology

This Good Clinical Practice Recommendation (GCPR), initiated by the Indian Society of Assisted Reproduction (ISAR), provides evidence-based recommendations for improving Assisted Reproductive Technique (ART) outcomes with the use of adjuvants. The coordinators of this expert opinion formulation, i.e., Dr. Ameet Patki, Dr. Asha Baxi, Dr. Fessy Louis, Dr. Niharika Tyagi, Dr. Mrinmayi Dharmadhikari, and Dr. Ashish Gude, formulated and finalized 10 key questions addressing crucial areas such as patient profiles for adjuvants and adjuvant strategies, optimal dosing, and duration of adjuvant therapy to improve ART outcomes. Fifty-one infertility specialists invited by ISAR gathered at Radisson Blu, Goa, to discuss these questions, sharing clinical insights. The resulting expert opinion offers comprehensive, evidence-based recommendations to improve outcomes and overall well-being in women with infertility.

Patient Profiles and Corresponding Adjuvant Strategies in ART/IVF

1. Do adjuvants have a role in Poor Ovarian Responder (POR) patients undergoing ART/IVF, and how can it be individualized among patient profiles?

- POR are women showing a suboptimal response to ovarian stimulation (OS). They often have multiple factors affecting fertility and pregnancy outcomes.
- The POSEIDON (Patient-Oriented Strategies Encompassing Individualize D Oocyte Number) criteria were introduced to better classify this heterogeneous group. It divides patients into four subgroups based on age, ovarian reserve (AFC/AMH*), and prior stimulation response, helping guide tailored treatment strategies.
- POSEIDON groups 1 and 2 include patients with good ovarian reserve but a poor ovarian stimulation (OS) response, likely due to reduced follicular sensitivity to Follicle-stimulating hormone (FSH). The goal is to improve oocyte yield and obtain at least one euploid blastocyst. Evidence suggests that Dehydroepiandrosterone (DHEA) pre-treatment, along with strategies such as using recombinant FSH, higher FSH doses, adding recombinant Luteinizing hormone (LH), or applying a DuoStim protocol, may enhance outcomes.
- POSEIDON groups 3 and 4 include women with diminished ovarian reserve (AFC < 5 or AMH < 1.2 ng/mL). Group 4 also faces age-related oocyte quality decline. Management aims to optimize oocyte yield and quality through individualized stimulation, tailored ovulation triggers, and possible adjuvant therapies like DHEA, growth hormone (GH), and antioxidants (Coenzyme Q10 (CoQ_{10}), resveratrol, melatonin), though stronger evidence is needed.

Commonly used adjuvants in POR patients

- Preclinical data indicate DHEA promotes granulosa cell growth, enhances FSH response, and improves follicle recruitment. A 2023 meta-analysis showed DHEA increases Antral follicle count (AFC), lowers FSH, reduces gonadotropin use, and decreases miscarriage rates, though clinical pregnancy and Live Birth Rates (LBR) benefits were seen only in non-RCTs. Evidence remains limited, warranting cautious use.
- GH may improve receptor expression, mitochondrial activity, and oocyte quality, potentially increasing oocyte yield and Clinical Pregnancy Rate (CPR) in poor responders, but effects on LBR are inconsistent—routine use is not yet supported.
- CoQ_{10} pretreatment in diminished ovarian reserve improves oocyte yield, embryo quality, and pregnancy rates while reducing stimulation duration, dose, and miscarriage risk, though data remain insufficient for routine use.
- Resveratrol may enhance mitochondrial and follicular function and protect against ovarian aging via SIRT1 activation, but clinical validation is lacking.

Expert Recommendations:

Various adjuvants (e.g., DHEA, GH, CoQ_{10}, resveratrol, etc.) have shown potential in improving outcomes in POR patients, though high-quality evidence remains limited. Their selection should be based on efficacy and tolerability, guided by clinician experience, and tailored to the POSEIDON group. A potentially beneficial role of DHEA for groups 1 and 2, growth hormone for groups 3 and 4, and CoQ_{10} or resveratrol across all POSEIDON groups has been observed.

2. Do adjuvants have a role in Polycystic Ovary Syndrome (PCOS) patients undergoing ART/IVF, and how can it be individualized among patient profiles?

- In PCOS, infertility mainly arises from ovulatory and implantation issues linked to chronic inflammation, immune imbalance, oxidative stress and metabolic dysfunction (e.g., Insulin resistance, Obesity, hyperandrogenism). Adjuvant therapies targeting these factors may help improve fertility, though strong evidence is limited (Fig. 1).
- Management also includes lifestyle changes, ovulation induction (letrozole, clomiphene, gonadotropins), and progesterone for luteal support. All those who show insulin resistance assessed with a positive glucose challenge may be prescribed metformin/ inositols; selection of adjuvants can be individualized based on PCOS phenotype for targeted treatment; (Table 1).

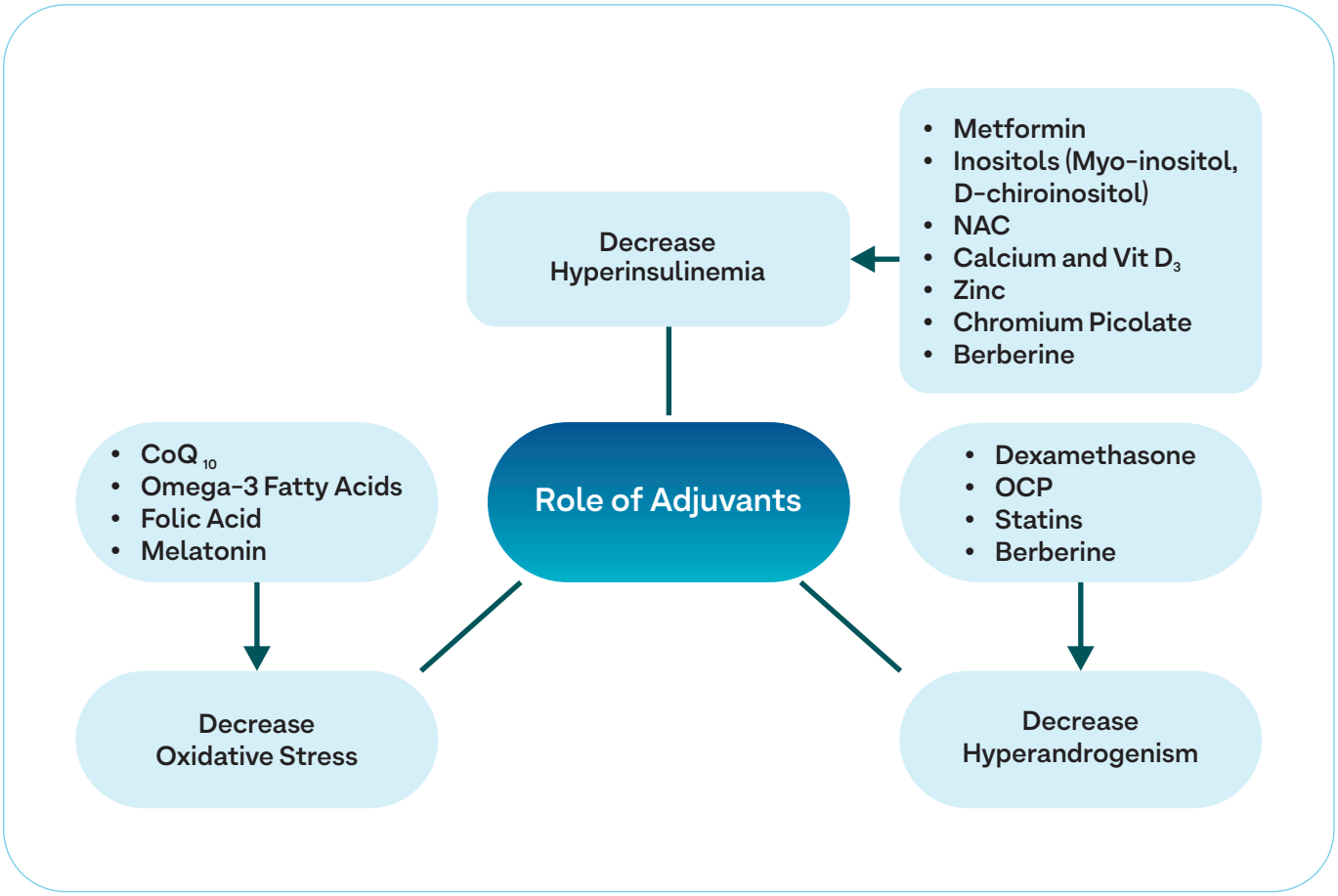

Fig. 1: Role of Adjuvants in PCOS Management,
NAC: N-acetylcysteine, OCP: Oral Contraceptive Pills

Table 1: PCOS Phenotypes: Clinical Features and Corresponding Adjuvant Therapies

Types of Phenotypes	Features	Clinical profile	Suggested Adjuvants
Phenotype A	Hyperandrogenism + Ovulatory dysfunction + Polycystic ovarian morphology	Considered a severe form of PCOS, often associated with obesity, insulin resistance, and significant metabolic dysfunction	Insulin-sensitising agents (metformin, inositols, berberine), antioxidants (CoQ_{10}), and ovulation induction agents (letrozole, clomiphene citrate (CC), gonadotropins) with weight management.
Phenotype B	Hyperandrogenism + Ovulatory dysfunction; no polycystic morphology on ultrasound		
Phenotype C	Hyperandrogenism + Polycystic ovarian morphology; regular ovulation	Milder clinical and endocrine alterations	Limited role of adjuvants. Inositols, CoQ_{10}, Vitamin D (if metabolic dysfunction present), and berberine may be considered.
Phenotype D	Ovulatory dysfunction + Polycystic ovarian morphology; no hyperandrogenism	Milder clinical and endocrine alterations	Limited role of adjuvants. Inositols, CoQ_{10}, Vitamin D (if metabolic dysfunction present), and berberine may be considered.

Expert Recommendations:

Patients with PCOS who present with ovulatory dysfunction, low progesterone, metabolic abnormalities, obesity, insulin resistance (assessed with a positive glucose challenge), or hyperandrogenism are likely to benefit from adjuvant therapy. Phenotype A and B may benefit from insulin sensitizers and weight-reduction agents (e.g., metformin, berberine, inositols, etc.), ovulation induction (e.g., letrozole, CC, etc.), and antioxidants (e.g., CoQ_{10}) while Phenotype C may require the use of ovulation induction agents, while other adjuvants (e.g., CoQ10, berberine, inositols, vitamin D, etc.) can selectively be considered in Phenotypes C and D, depending on individual patient profile.

3. Do adjuvants have a role in Recurrent Implantation Failure (RIF) patients undergoing ART/IVF, and how can it be individualized among patient profiles?

- The European Society of Human Reproduction and Embryology (ESHRE) defines Recurrent Implantation Failure (RIF) as repeated failure of viable embryo transfers to achieve pregnancy, warranting further evaluation. Successful implantation requires a healthy embryo, receptive endometrium, and proper embryo–endometrium interaction.

- Couples with ≥2 failed transfers and >60% cumulative implantation probability should be counselled for additional tests and treatments. Causes include immune, thrombotic, endometrial, anatomical, infectious, and hormonal factors, which can guide personalized adjuvant strategies to improve ART/IVF outcomes (Table 2).

Table 2. Summary of etiologies and treatment/adjuvant options of recurrent implantation failure

Factors	Treatment/Suggested Adjuvants	Evidence
Risk factors		
Obesity, Smoking, Alcohol, Stress	Stop smoking and alcohol intake, healthy diet, regular exercise, etc.	While association studies abound, evidence from well-designed intervention studies following short and/or long-term lifestyle changes remains scarce.
Maternal factors		
Advanced Maternal Age (> 35 years) (Decreased oocyte and embryo quality, endometrial receptivity, etc.)	Antioxidants (CoQ_{10}, Resveratrol, Melatonin etc.), Assisted Hatching (AH), etc.	Antioxidants can improve gamete quality &endometrial response, while AH may help improve implantation rates. However, current evidence in RIF patients remains limited.
Immunology	Glucocorticoids, Intravenous immunoglobulin (IVIG), Tacrolimus, Cyclosporine, Intralipids	Immunomodulatory effects by neutralizing auto-antibodies, lowering elevated Th1/Th2 ratio, and reducing NK cell activity. However, evidence remains limited, with small studies and non-RIF-specific populations.
	CoQ_{10}	Has been shown to support immune homeostasis by reducing elevated Th1 levels in patients with recurrent pregnancy loss. Since elevated Th1 responses are also implicated in RIF, CoQ_{10} may play a beneficial role.
Thrombophilia	Aspirin, Low molecular weight heparin (LMWH)	Aspirin has not shown significant benefits in implantation or pregnancy rates. LMWH appears to improve LBR in acquired thrombophilia patients, though its use in RIF remains based on limited, heterogeneous data.
Endometrial receptivity	Estrogen	If thin endometrium, sufficient exposure to estradiol by augmenting oral therapy with patches or vaginal treatment remains the mainstay of management.
	Peripheral blood mononuclear cells, Granulocyte colony-stimulating factor, etc.	Largely empirical, with unclear mechanisms and insufficient safety and efficacy data to support routine use.
Chronic Endometritis	Antibiotics	Can be considered.
Male factors		
Semen Quality	Antioxidants (CoQ10, L-carnitine, Astaxanthin, Lycopene, etc.), Sperm Selection (Intracytoplasmic morphologically selected sperm injection, testicular sperm extraction, etc.)	Have shown improvement in semen parameters, including motility, concentration, DNA Fragmentation, etc., and selection of`functional sperm; however, data in RIF populations remain limited.
Embryo Factor	Assisted hatching (AH)	Insufficient evidence in RIF patients.

Expert Recommendations:

Adjuvant therapies for RIF patients can be tailored to specific underlying causes. Lifestyle modifications and antioxidants (e.g., CoQ_{10}) can be helpful in those with risk factors such as smoking, advanced age, or obesity; immune-related issues may be addressed with glucocorticoids, IVIG, or CoQ_{10}; thrombotic tendencies with aspirin and LMWH; endometrial receptivity with estrogen; embryological concerns with lab techniques like AH; and male factor issues with antioxidant support or functional sperm selection.

However, most of these approaches lack robust RIF-specific evidence, underscoring the importance of individualized application and the need for further high-quality trials.

4. Do adjuvants have a role in unexplained infertility patients undergoing ART/IVF, and how can it be individualized among patient profiles?

- ESHRE defines unexplained infertility as infertility in couples under 40 with normal reproductive anatomy, function, and coital frequency but no identifiable cause. Management is largely empirical. Oxidative stress is a key factor, with markers like elevated Malondialdehyde (MDA) linked to poor oocyte quality and implantation.
- Antioxidants (CoQ_{10}, resveratrol, melatonin, vitamins C/E, NAC, alpha-lipoic acid) may help by improving mitochondrial function and reducing free radical damage, especially in patients with oxidative stress from obesity, smoking, or alcohol use.
- First-line management includes ovarian stimulation (clomiphene or letrozole) with Intrauterine Insemination (IUI) for 3–6 cycles, followed by IVF if unsuccessful.
- Due to IVF's variable success and high cost, adjuvants—medical, laboratory, or complementary are often used to enhance outcomes.
- Adjuvant choice depends on patient profile: CoQ10 or DHEA for older women, GH or androgens for poor responders, and targeted therapies (e.g., estradiol, antioxidants, aspirin, LMWH, IVIG, Granulocyte Colony-Stimulating Factor (G-CSF)) for specific ART failures, though supporting evidence remains limited.

Expert Recommendations:

In patients with unexplained infertility, ovarian stimulation agents (e.g. CC, letrozole) are preferred. Antioxidants (CoQ_{10}, resveratrol, melatonin, etc.) may be added as oxidative stress has been linked to unexplained infertility. Additional adjuvants (e.g., GH, DHEA, etc.) can be selected based on clinical factors such as age, ovarian reserve, and prior ART outcomes.

5. Do adjuvants have a role in male infertility patients and how can it be individualized among patient profiles?

- Male infertility is multifactorial, often linked to oxidative stress, metabolic dysfunction, and poor sperm quality. Excess Reactive Oxygen Species (ROS) damages sperm DNA, lipids, and proteins, impairing fertility. Antioxidant-based therapies for 3–6 months can safely improve sperm function and outcomes.
- Demographic & Lifestyle Factors: Advanced paternal age (>40 years) and unhealthy habits (smoking, alcohol, obesity, stress) increase ROS and DNA damage. Antioxidants (CoQ_{10}, zinc, selenium) and motility enhancers (pentoxifylline) may improve sperm quality, while lifestyle modification remains essential.
- Laboratory Parameters: Abnormal semen analysis (low count, motility, morphology) or high DNA fragmentation may benefit from CoQ_{10}, zinc, selenium, lycopene, and L-carnitine. In hormonal imbalance, nutraceuticals like Tribulus terrestris, L-arginine, myoinositol, and antioxidants can aid spermatogenesis and erectile function.
- Clinical Profile: Conditions such as varicocele or metabolic disorders (obesity, diabetes, hypertension) contribute to oxidative stress and impaired sperm function. Management of comorbidities plus antioxidants (CoQ_{10}, astaxanthin) can improve outcomes. Empirical antioxidant or hormonal therapy may also help in idiopathic infertility.

Expert Recommendations:

Adjuvant therapies including antioxidants (e.g., CoQ_{10}, myoinositol, L-carnitine, lycopene, selenium, astaxanthin) and nutraceuticals (e.g., Tribulus Terrestris, Ecklonia Bicyclis, Chitosan Oligosaccharide, etc.) can be beneficial in male infertility cases when patient-related factors (e.g., advanced age, obesity, smoking, etc.), laboratory abnormalities (e.g., Oligoasthenoteratozoospermia (OAT)), or clinical co-morbidities (e.g., erectile dysfunction, varicocele, etc.), compromise sperm quality and reproductive potential.

1. Is the use of a single adjuvant sufficient in most IVF cases, or is there a need to consider combination therapy for optimal outcomes?

- Despite over 8 million IVF births worldwide, live birth rates (LBRs) per cycle remain low (19–22%), causing emotional and financial strain. To improve outcomes, clinics increasingly offer adjunctive or "add-on" treatments-optional steps added to standard IVF to enhance specific aspects of fertility care.
- In women, adjuvant therapies can improve follicular recruitment, oocyte quality, and implantation rates, while helping regulate insulin resistance and hormonal balance, especially in PCOS.
- In men, adjuvants may enhance spermatogenesis and spermiogenesis, improving sperm count, motility, and morphology. Despite growing evidence and popularity, selecting a single or combined adjuvant remains complex and depends on individual pathology and treatment goals.
- Oxidative stress is a key mechanism in reproductive aging and diminished ovarian reserve. With age, CoQ_{10} and antioxidant enzymes like Catalase, SOD, and GPX decline, reducing ovarian defense against Reactive Oxygen Species (ROS) and lowering oocyte quality.
- CoQ_{10}, a bioenergetic antioxidant, supports ATP synthesis and mitochondrial activity, improving oocyte yield, embryo quality, and CPR while reducing cycle cancellations and miscarriages.
- Other adjuvants such as Omega-3 fatty acids, lycopene, and selenium (Se) have also shown promise.
- Omega-3 PUFAs support prostaglandin synthesis and hormonal regulation, improving uterine function and embryo quality. In PCOS, supplementation has been shown to lower LH levels, improve insulin sensitivity, reduce inflammation, and enhance ovulation.
- Selenium contributes to follicular redox balance, inhibits inflammatory cytokines via NF-κB suppression, and activates Nrf 2 antioxidant pathways.
- Lower Se levels have been linked to endometriosis and hyperandrogenism in PCOS.
- In male infertility, oxidative stress also plays a major role. Targeted antioxidant therapy—CoQ_{10} or L-carnitine for poor motility, zinc for morphology defects, astaxanthin for acrosomal function, and L-arginine for sexual dysfunction- can improve outcomes.
- Combination adjuvant therapies may better mimic natural biological interactions and offer synergistic effects, particularly in individuals with high oxidative stress, obesity, or metabolic dysfunction.

Expert Recommendations:

The choice between single and combination adjuvant therapy in IVF should be guided by the patient's clinical profile. For a single, well-defined etiology, a targeted adjuvant may be sufficient. In cases with multiple pathophysiological mechanisms or in those with co-morbidities, a combination approach is preferred to address the various contributing factors and optimize outcomes.

2. What clinical or laboratory criteria should guide the decision to combine two or more adjuvants versus using a single agent?

Decision Framework for Combination vs. Single Adjuvant Therapy

- The choice between combination adjuvant therapy and monotherapy should be guided by a comprehensive assessment of clinical presentation and laboratory findings.

Single vs. Multifactorial Profiles:

- Patients with a single, well-defined infertility cause may respond to monotherapy, whereas those with multifactorial etiologies, comorbidities, or multiple risk factors often benefit from combination therapy.
- For example, women of advanced maternal age with poor oocyte quality may use Coenzyme Q10 (300–600 mg) alone to support mitochondrial function. However, if accompanied by obesity and higher oxidative stress, combining CoQ10 with myo-inositol can enhance both antioxidant protection and metabolic control.
- Similarly, men with mild varicocele may respond to CoQ10 alone, but smokers or those with multiple oxidative risk factors may require combination antioxidants such as lycopene, omega-3s, or selenium for broader protection.

Inadequate Response to Monotherapy:

- If no significant improvement occurs after 8–12 weeks or three treatment cycles, additional agents with complementary mechanisms may be introduced.
- For instance, adding resveratrol to CoQ10 in older women may improve telomere stability, while combining CoQ10 with lycopene or L-carnitine in men may enhance sperm DNA integrity through synergistic antioxidant effects.

Laboratory Indicators

Hormonal and Reproductive Markers:

- Routine markers—prolactin, estradiol, FSH, LH, testosterone, Anti-Müllerian hormone (AMH), AFC, Follicular Output Rate (FORT), Follicle-to-Oocyte Index (FOI), and semen analysis- help determine therapy type. A single abnormality often warrants targeted monotherapy, whereas multiple or partially improved parameters suggest combination therapy.
- For example, women with low AMH but good follicular response may benefit from CoQ10 alone, while those with low AMH and poor FORT may require CoQ10 + myo-inositol.
- In men, isolated motility defects respond to L-carnitine, while those with DNA fragmentation may need CoQ10 + lycopene.

Oxidative Stress Markers:

- Tests such as ROS, lipid peroxidation, Total Antioxidant Capacity (TAC), and oxidation-reduction potential (ORP) can guide escalation. Persistently elevated oxidative markers indicate multi-pathway damage that may need combined antioxidants.
- For example, women with high ROS may use lycopene, while those with lipid peroxidation may need CoQ10 + lycopene; in men with DNA fragmentation and severe oxidative stress, L-carnitine + astaxanthin may be more effective.

Other Specialized Tests:

- Less common investigations—such as immune (e.g., antiphospholipid antibodies, NK activity) and genetic markers (e.g., Y-chromosome microdeletions)—can further refine therapy.
- For example, in recurrent pregnancy loss linked to immune imbalance, CoQ10 may help restore the Th1/Th2 ratio; in men with antisperm antibodies, combining antioxidants with immunomodulatory agents may improve sperm function.

Expert Recommendations:

The decision to move from single agent to combination adjuvant therapy should be guided by a combination of clinical findings and laboratory parameters that reflect disease intensity and complexity (e.g., endocrine, immunological, and redox imbalance markers). Single-agent adjuvant therapy may be considered when clinical findings or laboratory parameters indicate a mild, isolated abnormality. Combination therapy is preferred when multiple domains, immunological, oxidative stress, etc., are concurrently deranged, reflecting a more complex pathophysiology.

3. When should adjuvant therapy ideally be initiated before IVF (oocyte pickup or embryo transfer) to achieve optimal clinical benefit? Until what point in the IVF cycle—oocyte retrieval, embryo transfer, or early pregnancy—should adjuvant therapy be continued, and what does evidence support as best practice?

- In assisted reproductive technology (ART), adjuvant therapies are increasingly used to enhance oocyte quality, endometrial receptivity, and overall IVF success.
- The timing of initiation is critical, as each adjuvant acts during specific phases of follicular development, oocyte maturation, or endometrial preparation.
- Based on duration and biological effect, adjuvants are classified as long-term or short-term.
- Long-term adjuvants are started weeks to months before ovarian stimulation to influence folliculogenesis (≈3 months) and improve oocyte quality and ovarian reserve.
- CoQ10 enhances ovarian response and oocyte mitochondrial function, restoring cumulus cell activity and improving reproductive performance when taken 3–6 months before stimulation.
- Resveratrol may improve ovarian function and oocyte quality while protecting against age-related fertility decline. However, due to its potential negative effects on endometrial decidualization, it should be discontinued after oocyte retrieval.
- Short-term adjuvants are administered during stimulation or around embryo transfer to support endometrial preparation and implantation.
- Aspirin may improve uterine blood flow and endometrial receptivity by reducing platelet aggregation and vasoconstriction. The EAGeR Trial found that starting aspirin at the beginning of the IVF cycle enhanced endometrial vascularization and improved implantation and pregnancy rates.

A summary of adjuvants with recommended dosing protocols is provided in Table 3.

Adjuvant	Protocol
Antibiotics	Doxycycline 100 mg for 4 days beginning from vaginal egg pick up (VPU) [or] Azithromycin lg given on the night before VPU [or] Augmentin duo forte BD for 4-5 days post-VPU
Aspirin	100 mg from VPU until pregnancy test
Enoxaparin / Heparin	20-40 mg from VPU until pregnancy test
Steroids	Various protocols - 10-30 mg daily Used from stimulation until - Some stopping at pregnancy test - Some stopping until the 1" trimester
Melatonin	4 mg given at night Variable start time, but between 2 days and up to 8 weeks before egg collection Ceased on egg collection
Dopamine agonist	0.5 mg cabergoline orally daily From day of hCG or egg pick up and continuing to 5 days or until pregnancy test [or] Bromocriptine 7.5 mg oral starting with hCG trigger until pregnancy test
HCG infusion	Dilution of 1500 IU of hCG in 125 microlitres of blastocyst media, 40 microlitres of this was infused into the uterus 10 min to immediately prior to embryo transfer
DHEA	75 mg daily Given for 3 mths prior to cycle
Testosterone	Given as pre-treatment between 5-21 days before the start of a cycle Given as either a 2.5 mg patch or 10 mg topical gel
Growth hormone	12 IU/day from day of FSH until trigger injection Intramuscular injection
Intralipid infusion	200 mls of Intralipid 20% was given intravenously over two hours 7-10 days before embryo transfer. When a pregnancy was confirmed, additional doses were administered at 7, 9, 11 and 13 weeks
Filgrastim	Intrauterine Given 2 days before Embryo Transfer (ET) 300 µg into uterus 2 days before ET
Co-enzyme Q10	150-300 mg given at night Variable start time, but between 2 days and up to 8 weeks before egg collection Ceased on egg collection

Expert Recommendations:

Long-term adjuvants (CoQ10, resveratrol, melatonin, etc.) should be initiated well before stimulation to optimize oocyte competence. Short-term adjuvants (steroids, anticoagulants, GH, etc.) are best introduced during stimulation or immediately before embryo transfer to support implantation and early pregnancy.

4. What dosing strategies should be followed for commonly used antioxidants (e.g., CoQ10, myo-inositol, Omega 3 Fatty Acids, Lycopene, Selenium, Astaxanthin, Tribulus Terrestris, Ecklonia Bicyclis, Chitosan Oligosaccharide), and how should these be tailored based on patient-specific factors such as age, BMI, or ovarian reserve?

- **Coenzyme Q10 (CoQ10)** - Women: 30–1200 mg/day; Men: 60–300 mg/day (divided doses); Start ≥3 months before ART; Higher oxidative stress or age may require higher lipid-based doses for better absorption.
- **Myo-Inositol (MI)** - Women/Men: 4 g/day (2 g twice daily).
- **Omega-3 Fatty Acids (EPA/DHA)** - Women: 1–4 g/day; Men: 400–1865 mg/day; Prefer krill oil; take with fat-containing meals; Duration: 12–32 weeks.
- **Lycopene** - Men: 4–8 mg/day for 3–12 months (optimal 30 mg/day); Women: 6 mg/day; Absorption decreases with age, BMI, or low-fat diets; take with lipids or tomato products.
- **Selenium (Se)** - Women/Men: 100–200 µg/day (often with vitamin E); Monitor for toxicity; prefer organic forms (selenomethionine, selenocysteine).
- **Astaxanthin** - Women: 6–12 mg/day for 6–12 weeks; Men: 4–12 mg/day for 90 days; Use natural sources (e.g., Haematococcus pluvialis) for better safety.
- **Tribulus Terrestris (TT)** - 1500 mg/day (500 mg × 3) for 8–12 weeks; Useful in older patients; in women, take during follicular phase (days 5–14); may combine with LH-raising agents for PCOS or low ovarian reserve.
- **Ecklonia Bicyclis (EB)** - Men: 300 mg/day, often combined with COS and TT; Enhanced formulations improve absorption.
- **Chitosan Oligosaccharide (COS)** - Men: 250 mg/day (with EB and TT); Low molecular weight forms preferred.

5. What dosing strategies should be followed for commonly used adjuvants (e.g., DHEA, Testosterone, Growth Hormone, Aspirin, Prednisolone), and how should these be tailored based on patient-specific factors such as age, BMI, or ovarian reserve?

- **DHEA - Dose:** 25 mg three times daily for 4–8 weeks or >50 mg/day; Adjustment: BMI affects response—low BMI patients show reduced androgen activity; high BMI shows smaller androgen increases.
- **Testosterone** - Men: Transdermal 2–6 mg/day; undecanoate (oral) 225–400 mg twice daily; gel 1% 50–100 mg/day or 1.62% 20–81 mg/day (male hypogonadism); Women: Transdermal patch 2.5–10 mg/day or oral undecanoate 40 mg/day for ≥40 days (poor ovarian responders); Adjustment: Greater benefit in men <40 yrs; efficacy consistent across BMI, though BMI ≥ 30 kg/m^2 may reduce sexual response.
- **Growth Hormone** - Women: 3–5 IU/day.

- **Aspirin -** Women: 75–100 mg/day (low-dose preferred).
- **Prednisolone** - Men: 12.5 mg/day; Women: 5 mg/day for 14–15 days post–embryo transfer.

Recommended Articles & Links

"Adjuvants in IVF — evidence for what works and what doesn't" by L. Nardo et al (2020); Link: https://doi.org/10.1080/03009734.2020.1751751;
"The use of adjuvants in assisted reproduction treatment" by R. Kennedy (2019); Link: https://journals.lww.com/grh/fulltext/2019/12000/the_use_of_adjuvants_in_assisted_reproduction.1.aspx;
"Adjuvant treatment strategies in ovarian stimulation for poor ovarian responders: a systematic review and network meta-analysis" by Y. Zhang et al (2020); Link: https://doi.org/10.1093/humupd/dmz046;
"Nutritional supplements and IVF: an evidence-based review" by R.J. Hart et al (2024); Link: https://www.rbmojournal.com/article/S1472-6483(23)00869-6/fulltext; "Clinical adjuncts in in vitro fertilization: a growing list" by M.S. Kamath et al (2019); Link: https://www.fertstert.org/article/S0015-0282(19)32375-1/fulltext

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***POR:** Poor Ovarian Response; ***OLS:** Omega-3 fatty acids, Lycopene & Selenium; ***PCOS:** Polycystic Ovary Syndrome

Indian Society For Assisted Reproduction

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