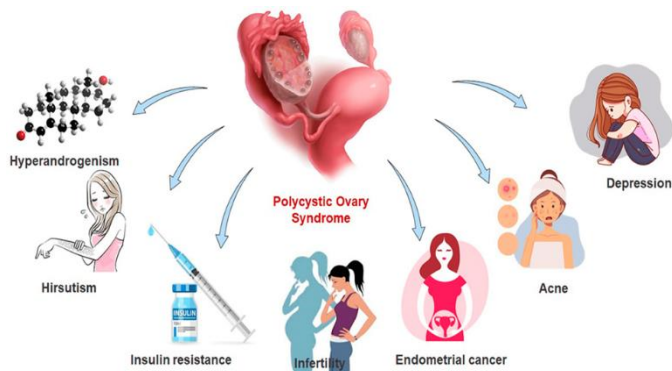


Emerging Therapeutic Strategies for PCOS Treatment

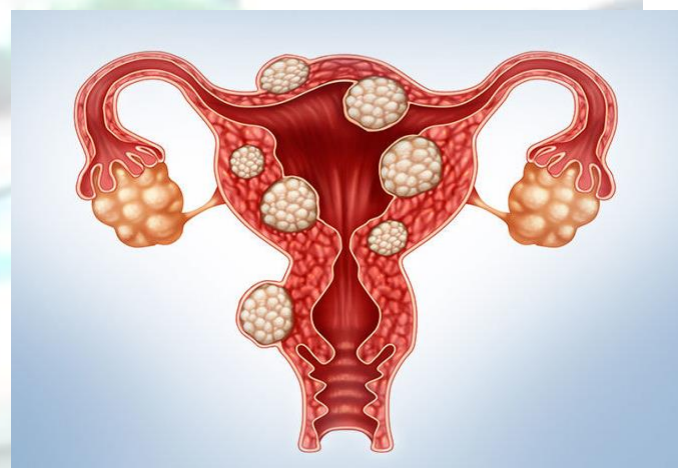


Polycystic ovary syndrome (PCOS) is one of the most common reproductive endocrine disorders in women which is characterized by chronic anovulation and ovarian dysfunction. This heterogeneous disorder can also be characterized by hyperandrogenism, menstrual irregularities and polycystic ovaries. PCOS is a leading cause of infertility because of lack of ovulation, which results in irregular periods and make it difficult to become pregnant. There are some other causes like excess androgen levels, cysts in the ovaries and hormonal imbalances.

In recent, it has become a significant public health problem which affects an estimated 8-13% of women of reproductive age and up to 70% of cases not well diagnosed. PCOS has a great impact in biological and psychological effects, these are related to obesity, body image and infertility. These can lead to mental health challenges and social stigma and causes anxiety, depression. In PCOS problem, women with a family history or type 2 diabetes are at higher risk. PCOS is a lifetime problem, so there is no cure for it, but treatments can improve symptoms. (World Health Organization: WHO & World Health Organization: WHO, 2023)

Ovulation inducement is the base of treatment for infertile PCOS patients who want to conceive as most of the women with PCOS has no ovulation problem. Clomiphene citrate is a selective estrogen receptor modulator (SERM). The preferred medication for ovulation induction in teenagers with polycystic ovarian syndrome is a clomid citrate (CC). (CC) functions as an anti-estrogen by blocking estrogen receptors in the hypothalamus, increasing the pulse width of gonadotropin-releasing hormone (GnRH) in the anterior pituitary, and boosting the synthesis of follicle-

stimulating hormone (FSH). Follicle formation is aided by the hormone luteinizing hormone (LH). Between the second and fifth day of the period, CC is typically administered for five days, starting at 50mg per day and gradually increasing to 150mg per day. About 80% of females ovulate after CC treatment. The CC effects were compared to placebo in three clinical trials in anovulatory women which results were summarized in a meta-analysis. In compared to placebo this meta-analysis revealed a greater clinical pregnancy rate in all CC treated groups. However, the two weeks extended half-life of this medication has long lasting effects on cervical mucus and endometrial growth. A dose up to 150mg/day for 5days up to at least three treatment courses has also been shown to be ineffective in 15%- 20% of PCOS afflicted women. For women with PCOS who are resistant to CC, CC can be given in addition to metformin (conditional evidence-based recommendations, moderate quality data). (Rababa'h et al., 2022)

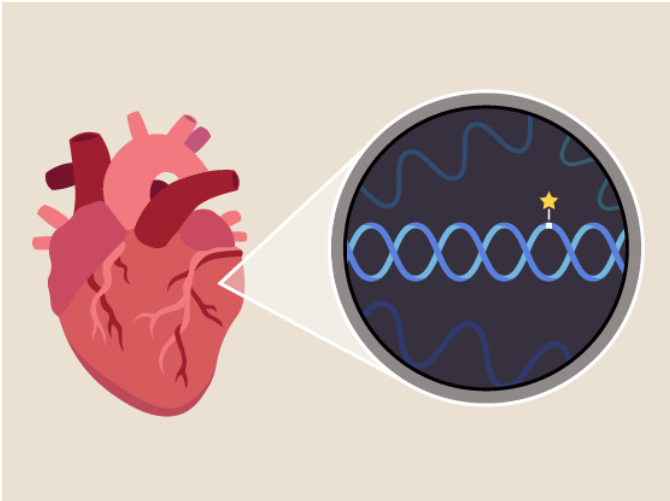


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CRISPR Gene Editing : A Novel Approach to Cardiovascular Diseases



decreased chance of developing heart disease. Even while CRISPR gene editing has a lot of potential, there are certain challenges. A possible problem is the difficulty of introducing the CRISPR-Cas9 system into the intended target cells in the body. Additional challenges include immunogenicity, potential off-target effects (caused by the Cas9 protein breaking DNA at unwanted locations), unwanted cell death. However, researchers are working to develop novel CRISPR-Cas9 delivery strategies that minimize off-target effects. Despite these challenges, CRISPR gene editing appears to have a bright future in the management of CVDs. With more research and development, this tactic might save millions of lives.

With 17.9 million fatalities a year, cardiovascular diseases (CVDs) constitute the primary cause of death globally. Because heart failure, strokes, and heart attacks are highly complex conditions with numerous risk factors, treating them can be challenging. Since many people are resistant to specific medications or therapies and standard procedures usually have limitations, innovative therapeutic options are required. CRISPR gene editing is a revolutionary method that may lead to the development of innovative therapeutics for cardiovascular disease. Genes may be precisely modified by scientists using the CRISPR-Cas9 technology. It works by adding to or deleting a segment of DNA that the guide RNA-guided Cas9 protein has cut at a specific spot. Heart disease is one of the several ailments that this treatment may be able to treat. CRISPR gene editing may be used to treat CVDs by focusing on genes linked to the development of atherosclerosis, an accumulation of plaque in the arteries that can cause heart attacks and strokes. For example, a recent study discovered that CRISPR-Cas9 may be used to change the gene encoding PCSK9, a protein that increases LDL (bad) cholesterol levels.

The study found that mice with modified PCSK9 genes had significantly lower LDL cholesterol levels and a lower risk of atherosclerosis. Another interesting approach is to modify genes linked to the development of CVDs using CRISPR. For example, a recent study showed that CRISPR may be used to modify the Toll-like receptor 4 (TLR4) gene, which codes for a protein associated with inflammation. The study found that after a heart attack, mice with altered TLR4 genes had a

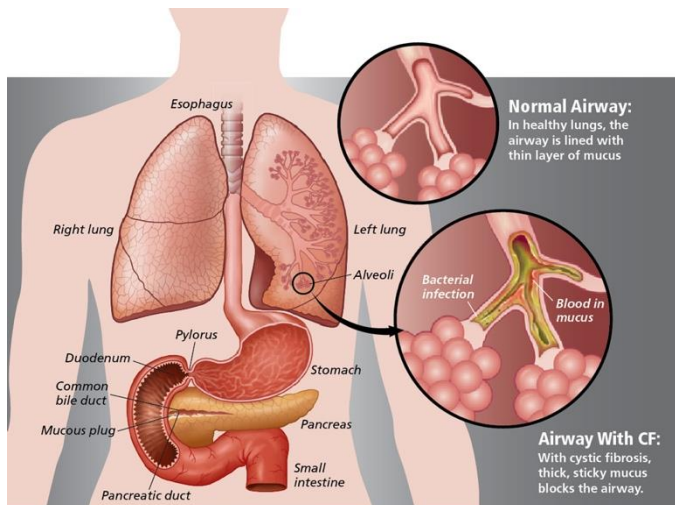


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Changes in Antibiotic Threats in CF: A Contemporary Challenge



Antibiotics have a crucial role in today's therapy for cystic fibrosis (CF), significantly contributing to the notable rise in median survival rates, which have reached almost 40 years. The outcomes of antibiotic therapy have a significant role in determining the quality of life, survival duration, and healthcare expenses associated with *P. aeruginosa* infections throughout early infancy. This includes the effectiveness of first and subsequent antibiotic treatment in eradicating these infections, as well as the efficacy of antibiotic treatment for respiratory exacerbations. Cystic fibrosis (CF) is an illness that affects several organs and is caused by mutations in the CF transmembrane conductance regulator (CFTR) gene. The disorder is complicated, diverse, and multi-organ.

Patients with cystic fibrosis are more likely to have *P. aeruginosa* isolates that are resistant to more than one drug and naturally resistant organisms like *Stenotrophomonas maltophilia*, *Achromobacter* (*Alcaligenes*) *xylosoxidans*, and non-tuberculous mycobacteria. This is likely due to the more effective treatment of the classic bacterial infection that is associated with CF. The *Staphylococcus aureus* infection is spreading more widely and displaying methicillin resistance. It is not known whether medication is the most effective for these antibiotic-resistant bacteria or even if treatment is always required. All of these conditions have the potential to be connected with either an asymptomatic infection or respiratory exacerbations in patients who have a chronic infection with significant numbers of these organisms. Similar to bacterial illnesses, fungal infections have become increasingly common in recent years. Infection with *Aspergillus* species has been

known for a long time to be a concern for cystic fibrosis patients. This infection often manifests itself as allergic bronchopulmonary aspergillosis.

Recent research has brought to light the possibility that an infection with *Aspergillus* might exacerbate respiratory conditions by inducing a kind of fungal-associated bronchitis that can be treated with specialised antifungal medications. Other fungi, such as *Scedosporium apiospermum* and *Wangiella* (*Exophiala*) *dermatitidis*, are becoming more acknowledged as factors that complicate treatment for cystic fibrosis patients.

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