

REGENERATIVE MEDICINE IN ANDROLOGY

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Introduction

Erectile dysfunction (ED) is a highly complex and multifactorial disorder that begins with endothelial dysfunction (ED fs), which is caused by reduced penile blood flow, arterial insufficiency or stenosis.

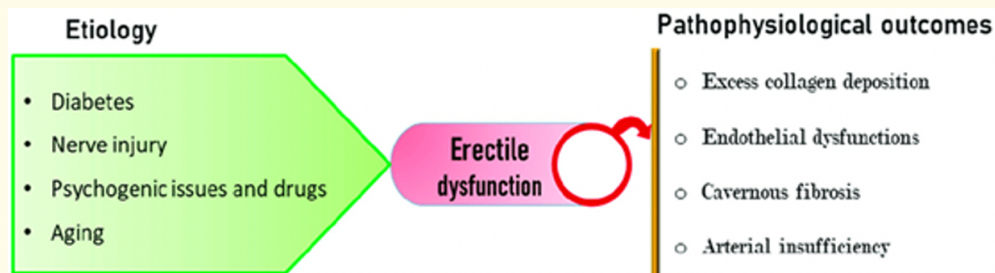


Figure 1: Pathophysiology of erectile dysfunction (ED).

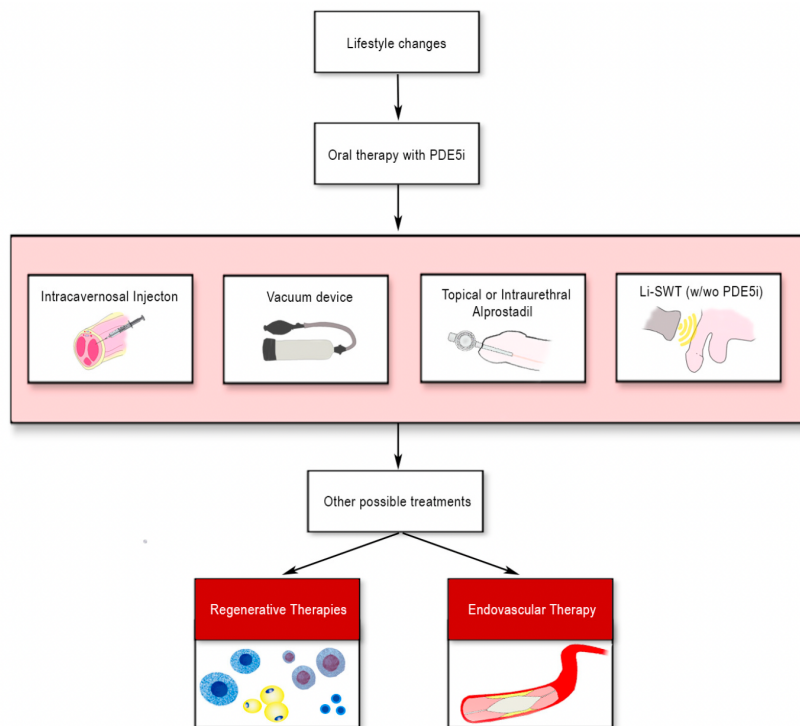
Most modern and recommended treatments can enhance erectile function by increasing blood flow without any influence on the underlying disease or on the pathophysiologic mechanisms leading to ED. The treatment of ED has mainly been based on the transient enhancement of penile erection but without a permanent reversal of endothelial dysfunction or restoration of the disturbed penile tissue homeostasis. ED is a prevalent sexual disorder among adult males and it has been traditionally associated with lower testosterone levels reported in elder males. However, recent epidemiological studies suggest an increasing incidence of ED in men younger than 40 years. Due to the complexity of erection, there are many potential mechanisms that can be involved; therefore, it is crucial to identify the specific causes of ED. Advances in diagnostic and treatment modalities offer opportunities to identify and manage young men with ED.

Furthermore, a growing number of patient suffering from vascular ED are becoming non responder to the common treatment such as phosphodiesterase-5 inhibitors (PDE -5is). Recently, alternative therapeutic strategies have been explored to treat non-responsive patients with vasculogenic ED.

However, even with the expansion of available treatments for ED, some patients still cannot achieve adequate performance. Surgical management with penile prosthesis implantation may be offered in patients who do not respond to second-line therapies. In this setting, diabetic patients are more than twice as likely to undergo penile prosthesis surgery than non-diabetics. Recently, alternative therapeutic strategies have been explored to treat non-responsive patients with vasculogenic ED effectively.



Current approaches to the treatment of erectile dysfunction

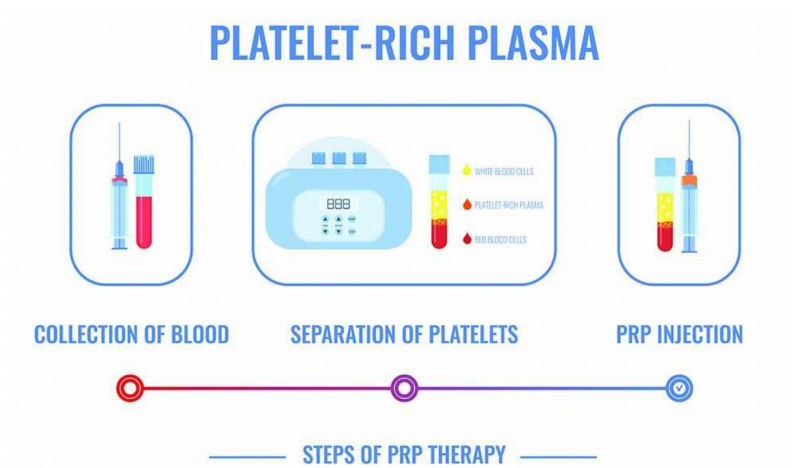


Regenerative medicine therapies

New available and effective strategies are cell-based regenerative therapies, including platelet-rich plasma (PRP) and peripheral blood mononuclear cells (PBMNC), highlighting the role played by immune cell populations, which may represent the new frontier of vasculogenic erectile dysfunction treatment.

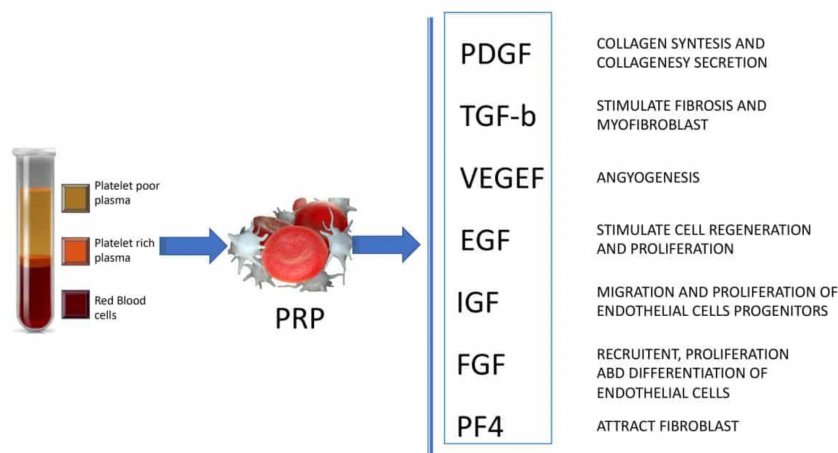
Platelet-rich plasma (PRP)

PRP is an autologous plasma fraction produced from the centrifugation of whole sample of blood that contains an average of 3- to 7-times higher mean platelet concentration compared to whole blood.



PRP injections became a treatment option in various medical fields, especially in orthopedics', because of the high concentration of growth factors they contain, such as, vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF). Several studies have demonstrated the potential of these growth factors in improving erectile function in both preclinical and clinical studies. Recently, there is a growing number of scientific studies supporting the use of intracavernous PRP injections as a promising, angiogenic and regenerative treatment modality for ED.

What is Platelet Rich Plasma!



The outcome is fundamentally improved blood stream to the penis, and great blood stream is vital for erectile capacity. Notwithstanding, the shot accomplishes something beyond improve the capacity to get an erection. PRP therapy is a sort of undifferentiated cell therapy. It not just improves blood stream but animates the growth of new cells in erectile tissues.

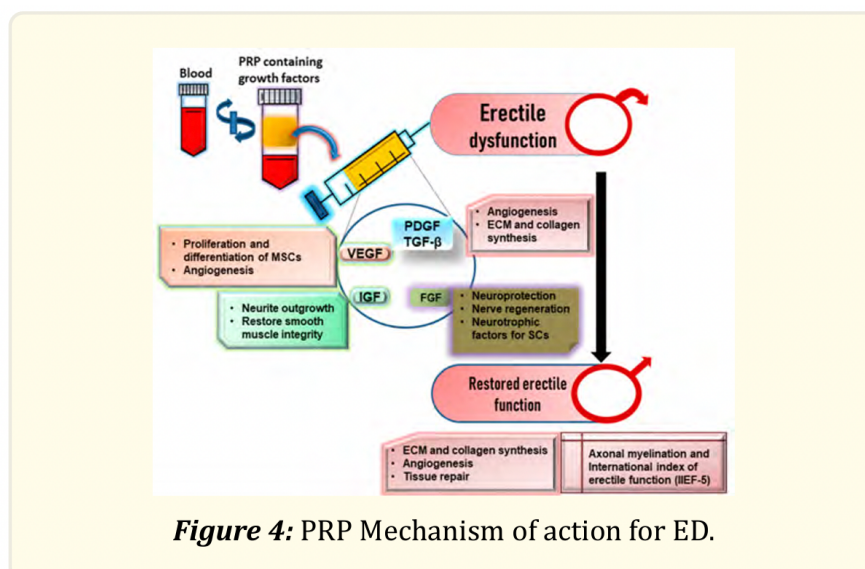


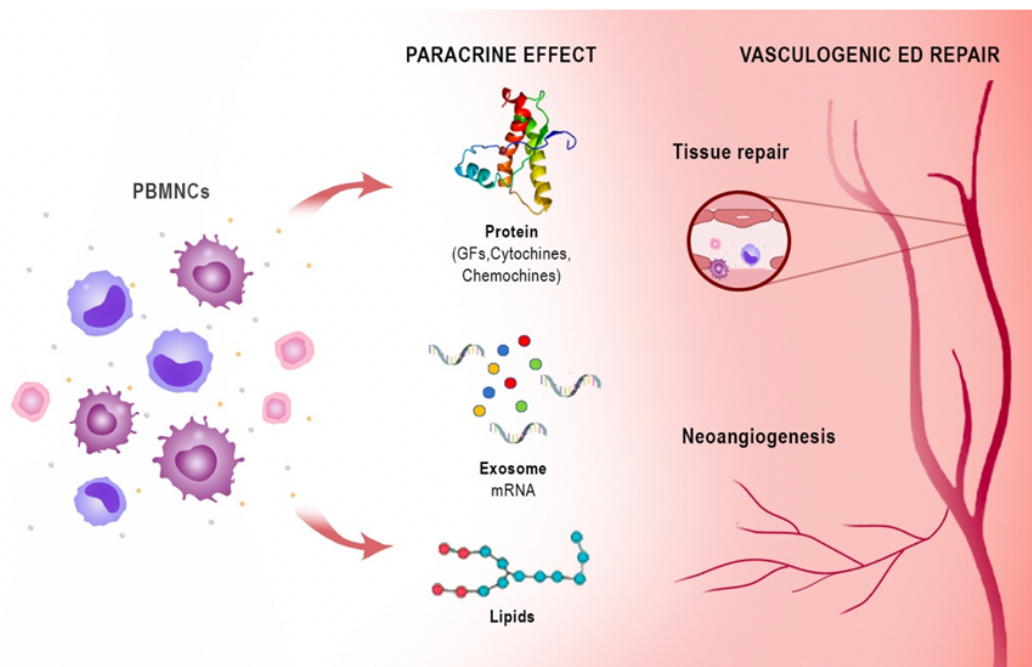
Figure 4: PRP Mechanism of action for ED.



Peripheral blood mononuclear cells (PBMNC)

Over the past few years, several studies have investigated the pre-clinical administration of stem cells (SCs) as a treatment for erectile dysfunction. SCs are undifferentiated cells capable of unlimited proliferation, multi-differentiation potency, and perpetual self-renewal. Preclinical research has shown that SCs exert their therapeutic effects based on active factors contained in their secretions that can act as messengers. Indeed, the effect of SCs has been shown to persist after their disappearance due to their pro-angiogenic, anti-inflammatory, anti-apoptotic, and anti-fibrotic properties.

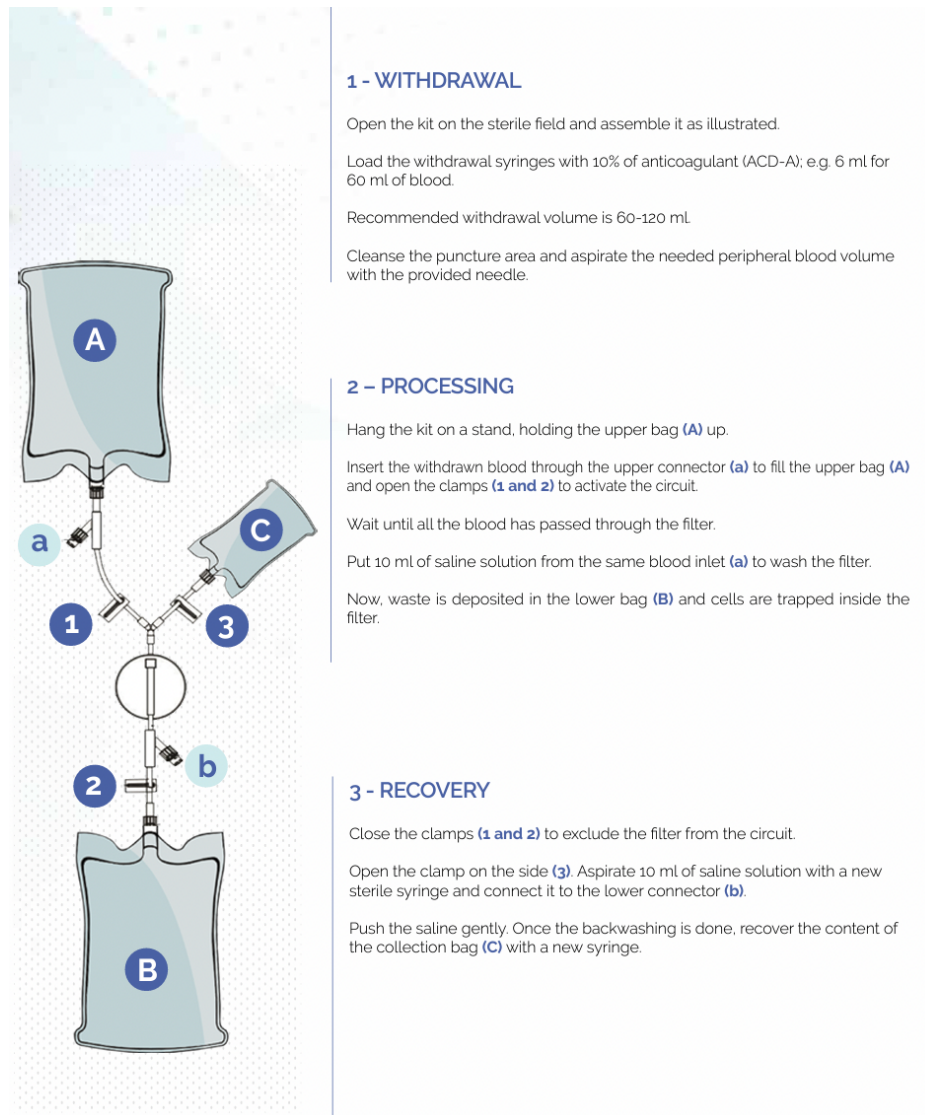
PBMNC secretome differs only slightly from the stem cell secretome in its ability to promote cell proliferation. These active paracrine factors, represented by different types of protein molecules, lipid mediators, microRNAs, and exosomes, underlie their generative effects of both stem cells and PBMNCs.



The immune system plays a critical role in tissue development, homeostasis and repair. Monocytes and macrophages are the first to respond to tissue damage and are required to successfully start the regeneration process. Through the release of chemokines, cytokines, matrix remodeling proteins and growth factors, they interact with the "niche of damage", i.e. the microenvironment where tissue damage occurred.



Collection of PBMNC is obtained by a closed filter system.



The technology filters blood through gravity, avoiding any act that could alter or stress cells (e.g. centrifugation). The core of the system is a membrane that can select cells by dimensional filtration, thus eliminating all the inflammatory cells such as granulocytes.



ERECTILE DYSFUNCTION TREATMENT

Regenerative procedures are every day more used to treat erectile dysfunction specially in case of diabetes and in case patients difficult to treat because they are, or they became poor/non responder to the classical treatment.

Dr. Davide Francomano protocol follow very precise steps to threat erectile dysfunction.

Step 1: blood test hormonal and metabolic parameters.

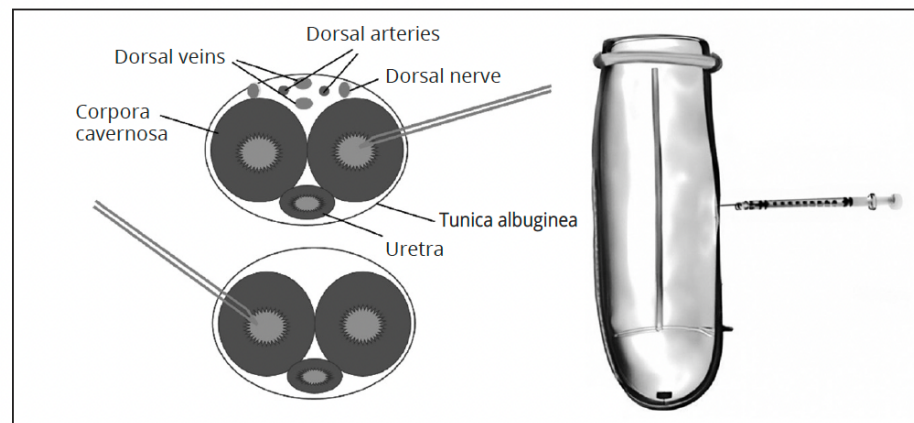
Step 2. Treat any metabolic imbalance (such as: trat hypogonadism, thyroid diseases or any other hormonal imbalance; improve glucose control and all the other metabolic parameters connected to Endothelial dysfunction and Erectile Dysfunction); also an appropriate supplementation therapy will be given each case to induce a better production of background molecules necessary for a better erection (improve Nitric Oxide, reduce oxidative status etc.).

Step 3. A Penile Doppler ultrasound will be performed to assess any vascular damage and the eventual presence of fibrotic tissue or Induratio Penis Plastica “IPP” (also known as Peyronie's disease).

Step 4. Regenerative treatment procedures injections personalized for each patient in base of all the previous conditions; the procedures can be performed into a single treatment or in a series of treatments depending on the gravity of the basal state.

Step 5. A second or more Penile Doppler ultrasounds will be performed to correctly access the state of treatment between any intracavernosal insertion.

Figure 1.—A) Schematic figure of injection site; B) intracavernous injections (injections need to be bilateral) latero lateral view.



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The penile injection will be performed in a surgical ambulatory equipped for small surgical procedures, each treatment will require one hour, and a light peripheral anesthesia will be given to the area before the intracavernosal injection.

