



Erectile Dysfunction: Old Question, New Answers and Ideas



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Many years ago, erectile dysfunction (ED) was defined as “the consistent inability to achieve an erection adequate for sexual intercourse.” From this philosophy came the goal of treatment of what was considered, essentially, a social disorder. The ultimate goal—give a man back his erection. A simplified chronological algorithm is depicted in Figure 1.

The development and introduction of oral agents led to a better understanding of what ED actually was. “The penis is a victim” became the initial theme. The Massachusetts male aging study estimated the true incidence of ED and suggested that if a man had certain conditions, he was more likely to have ED (as per Figure 2 and Table 1). Over the last 10 years, we have come to

realize that ED is not only a result of, but a precursor for, many conditions.

► Is there a link between ED and Metabolic syndrome?

The ED-metabolic syndrome link is becoming more than just a “pipe dream.” When a patient presents with ED, this link mandates an evaluation for:

- hyperglycemia,
- hyperlipidemia
- hypertension and
- obesity.

ED may very well be the “entry point” in male health issues.

Timeline	Treatment	Goal
<p>Desperation • Pre1960s</p> <p style="text-align: center;">↓</p> <ul style="list-style-type: none"> • 1960s • 1960s/70s • 1980s • Mid 1990s • 1998 <p>Expectation • 21st century</p>	<ul style="list-style-type: none"> • Early surgery/ natural remedies • Pumps • Implants • Prescribed injections • Intraurethral therapy • Oral agents • Future treatments 	<p>Any improvement</p> <p style="text-align: center;">↓</p> <p>Successful erection</p> <p style="text-align: center;">↓</p> <p>Normal sex life</p>

Figure 1. Evolution of the goal of erectile dysfunction (ED) treatment towards normal treatment.

Over the last 10 years, we have come to realize that ED is not only a result of, but a precursor for, many conditions.

Men 40 to 70 years-of-age

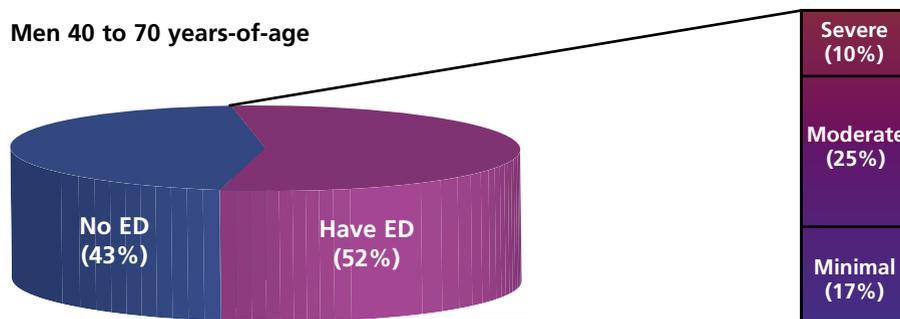


Figure 2. ED: Massachusetts Male Aging Study (MMAS).¹

Table 1

Conditions associated with ED

- Diabetes (complete ED in 28%)
- Heart disease (complete ED in 39%)
- Hypertension (complete ED in 15%)
- Low HDL-C levels
- Smoking (in men with heart disease or hypertension)
- Depression

Table 2

Why ED occurs sooner than cardiovascular (CV) disease

Artery	Diameter (mm)	Critical events
Penile	1 to 2 	ED
Coronary	3 to 4 	Angina/MI
Carotid	5 to 7 	Transient ischaemic attack/stroke



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Table 3

Link between ED and CV disease: A clinical study

Design

- A study of ED prevalence in 133 diabetic men with angiographically verified silent coronary artery disease vs. 127 diabetic men without myocardial ischemia at exercise or 48-hour ambulatory ECG and stress ECHO

Results

- Strong and independent association of ED with angiographically-verified silent CAD in men with uncomplicated Type 2 diabetes and a relatively low CAD risk
- ED affected one-third of patients with silent CAD and 5% without

Conclusion

- ED could be a potential silent CAD predictor

The development and introduction of oral agents led to a better understanding of what ED actually was.

► ***Is there evidence that ED is a precursor for endothelial dysfunction?***

Many studies have been done and are underway. Tables 2, 3, 4 and 5 provide some facts supporting this concept.

► ***Is there a link between testosterone and ED?***

Testosterone has been shown to be an essential component of erectile function, not just a stimulant for “sex drive” (Table 6).

The literature is replete with studies showing that Phosphodiesterase Type 5 (PDE5) failures can be salvaged with testosterone supplementation based on the fact that without the production of nitric oxide synthase, PDE5 inhibitors will not work. Adequate testosterone levels are essential for its synthesis.

Testosterone can also help down regulate the activity of the PDE5 enzyme in the penile smooth muscle cell, which is essentially how PDE5 inhibitors work.

Low testosterone levels have been shown to lead to the replacement of penile erectile smooth muscle cells with adipocytes and collagen.

Table 4

Vascular ED as a possible early marker of CV disease-part 1

Design

- A study of 300 men with angiographically-documented CAD

Results

- Prevalence of ED among patients was 49% (147/300)
- Among the 147 patients with coexisting ED and CAD, the onset of ED preceded CAD symptoms in 67% of patients (99/147)

Table 5

Vascular ED as a possible early marker of CV disease-part 2

Design

- A study of 137 men with ED on Doppler ultrasound

Results

- 96% had Doppler evidence of penile vascular disease, stratified as mild (11%), moderate (56%), or severe (29%)
- Correlation with C-reactive protein (CRP) was detected in men with ED, but no clinical detected CAD
- After adjusting for age, CRP was significantly associated with an increasing severity of ED

Table 6

Androgens and oral PDE5 therapy

- Nitric oxide synthase appears to be testosterone dependent
- Nitric oxide is necessary for PDE5 inhibitors to work
- Patients who fail oral PDE5 therapy should have determination and combined therapy considered
- Testosterone may be a “down regulator” of PDE5
- Important in cavernosal structure

PDE5: Phosphodiesterase Type 5

Table 7

Reasons for apparent treatment failure with oral therapy

- Inadequate dose
- Inadequate arousal or stimulation
- Inadequate timing between dose and attempted intercourse
- Not enough trials (reliability)
- Erectolytic factors outweigh the effect of oral therapy (stress, fatigue, alcohol)
- Testosterone supplementation
- Wrong diagnosis

PDE5 inhibitors are first-line ED treatment

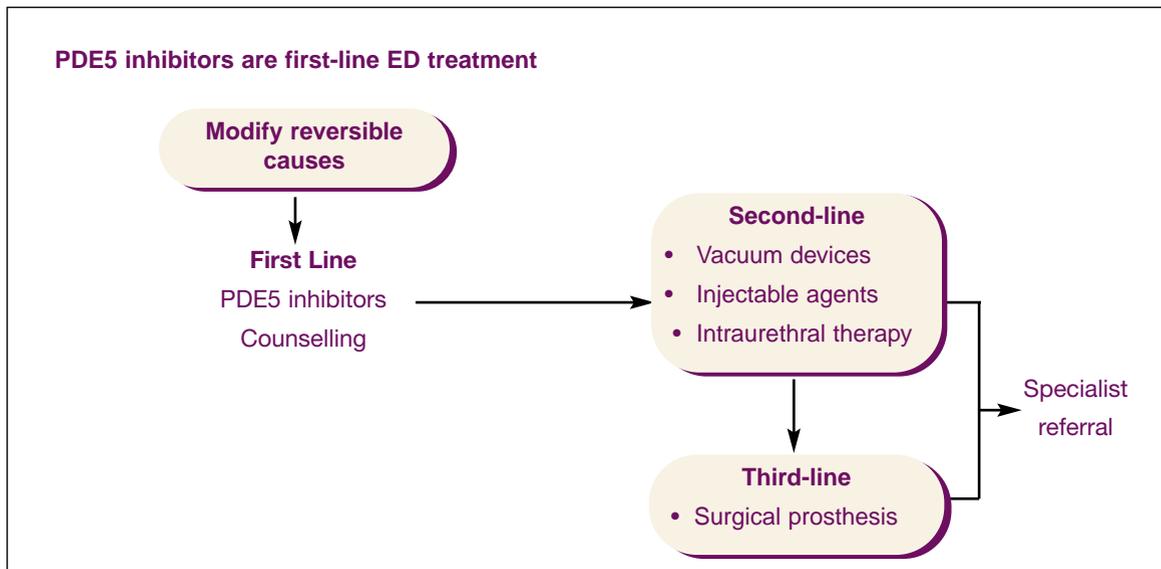


Figure 3. Second and third line treatments for patients who fail oral therapy.

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Take-home message

1. All ED patients must be investigated for diabetes, hyperlipidemia and hypertension on an ongoing basis
2. Management of lifestyle issues and control of comorbidities may improve ED
3. All ED patients should have a testosterone work-up
4. Maximize oral treatment success with maximum dosing, proper instructions and follow-up
5. Remember other treatment options for patients who fail or cannot take oral therapy

► How can one maximize treatment with oral ED medications?

A few simple rules will help to achieve success with oral ED medications (Table 7 demonstrates reasons for failure):

- Start with maximal doses of sildenafil
- Stimulation is necessary to “kick start” the erection (leads to nitric oxide release)
- Instruct patients to wait one hour the first couple of times they try to achieve an erection
- Try each pill three to four times before concluding treatment failure
- Arrange for follow-up appointments with all patients to reinforce the aforementioned
- Do not forget that there are second- and third-line treatments for patients who fail oral therapy (Figure 3)

Remember that many areas of the country have “ED experts”—not merely the average urologists—who are happy to see your patients.

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