Erectile Dysfunction:
A Predictor of Cardiovascular Health

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In March of 1998, sidenafil was launched in Canada. Since that time there has been the release of two other oral medications that have been proven effective for the management of erectile dysfunction (ED) in men. Sidenafil, vardenafil and taldalafil are being used extensively by men all over the world. All three are very effective in the right individual, while providing great safety and patient satisfaction, regardless of the underlying etiology of the problem.

Table 1

Factors associated with endothelial (erectile) dysfunction (dilation)

Hypercholesterolemia	1.71 RR
Hypertension	1.69 RR
Increasing age	-
Male gender	∞
Peripheral vascular disease	2.44 RR
Diabetes mellitus	3.72 RR
Tobacco use	2.41 RR
Hereditary predisposition	Unknown
Coronary artery disease (CAD)	1.61 RR
Drug intake	3.71 RR

RR: Relative risk of developing erectile dysfunction (ED).

ED

As shown in the Massachusetts Male Aging Study (MMAS), 52% of men between the ages of 40 and 70 will have some degree of ED.[1]

We know that ED, *per se*, is not life threatening, but it can threaten quality of life and relationships. The definition of ED being: "The inability to either obtain or maintain the erection for satisfactory sexual performance" has encouraged many more men, of even younger age, to declare their problem and seek some help with its management.

Previously, the concern was that we may have trivialized the diagnosis of ED, as it was viewed as a lifestyle issue. More recently, we have determined that this is not the case.

Sildenafil

It is interesting to note that originally, sildenafil was investigated as a drug to treat angina. Sildenafil, similar to other phosphodiesterase Type 5 (PDE5) inhibitors, has an impact on the preservation of nitric oxide that is naturally produced in the body under the influence of sexual stimulation. This nitric oxide is produced to start the conversion of guanosine triphosphate to cyclic guanosine monophosphate (cGMP). It is the cGMP that causes the dilatation of the

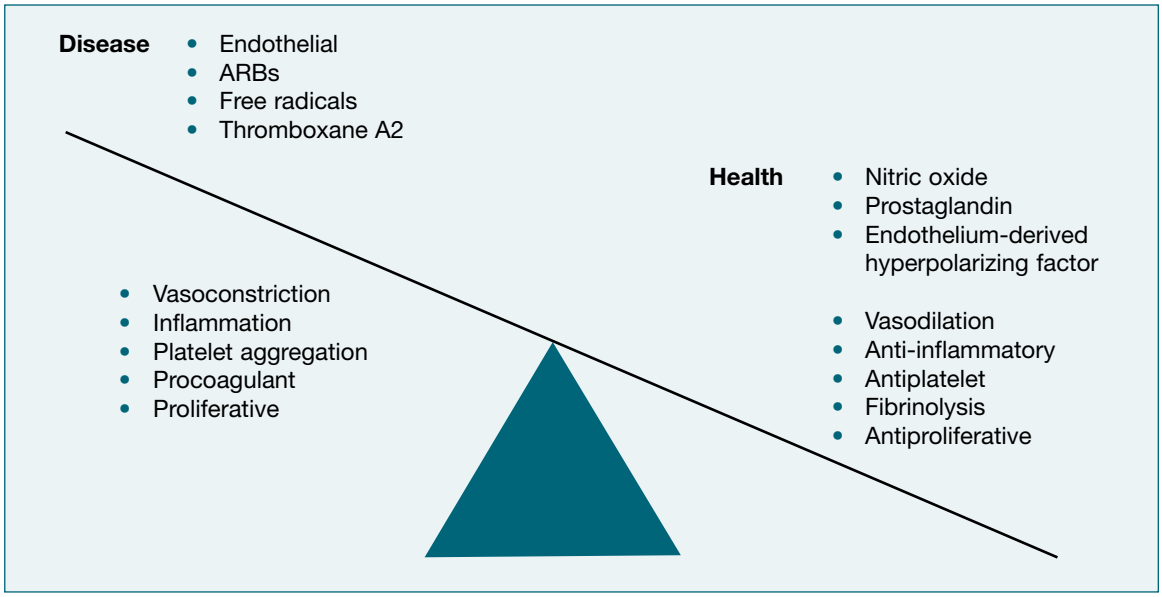

Figure 1. When is vascular homeostasis reached?

blood vessels leading to a bigger, stronger, longer erection. When the original work was being done, it was the thought that siladenafil would open up the coronary blood vessels as well. This would help to treat or prevent angina. Though it was seen that this was not the case, a number of the men were able to obtain erections that they had been unable to have for many years.

The discovery was that all blood vessels have an endothelial lining. Our new approach is to determine the relationship between endothelial dysfunction as well as ED. High nitric oxide levels are necessary for the integrity of vascular health.

Cardiovascular disease and ED

The MMAS shows a correlation between the risk factors associated with developing cardiovascular (CV) dysfunction as well as ED and that there is a significant overlap. All of the common factors that we can see (*e.g.*, smoking obesity, lack of exercise, lipid abnormalities, as well as diabetes) are the same factors on both sides of the problem.

As shown in the MMAS, 52% of men between the ages of 40 and 70 will have some degree of ED.

Having accepted the common risk factors that are shared by these two physiologic abnormalities, we can now identify the patient that is at high-risk for developing either ED or endothelial dysfunction (Table 1). Indeed, a number of studies have shown that the onset of ED can actually predate the development of CV dysfunction by months, if not years.

We have also seen that men diagnosed with diabetes will have a higher incidence of developing ED.[2]

The importance of diagnosing ED

Men that have already been diagnosed with ED have a very significant incidence of having simultaneous underlying CV disease. The discovery of the high incidence of silent coronary ischemia in those men that have been assessed or treated for ED should increase the importance and relevance of the diagnosis of ED. This would also bring the GP's annual history and physical examination to a new level (Figure 1).

Men that have already been diagnosed with ED have a very significant incidence of having simultaneous underlying CV disease.

More recent studies have proven the very strong relationship between endothelial dysfunction and ED (Table 2 and 3). It only makes sense that if the impact is on the endothelium that lines all of the blood vessels, then the smaller blood vessels would be affected first because they have less diameter to lose. A small amount of narrowing will cause a dramatic reduction of blood flow. Therefore, it behooves the FP to identify the "at-risk" patient by asking the question about ED. If the patient has no

Table 2

Vascular ED as a possible early marker of cardiovascular (CV) disease[4]

Results

- The prevalence of coronary artery calcification (CAC) was greater in ED patients than in controls
  - Mean CAC score of 143.3 in ED patients vs. 32.4 in controls (odds ratio: 2.57)
- In patients with ED, the prevalence and degree of multi-slice CT scan-detected asymptomatic atherosclerosis are significantly higher and not predicted by CV risk factors
- The ED subjects had significantly greater C-reactive protein levels and their endothelial-dependent flow-mediated dilatation was significantly impaired

Conclusion

- Vascular disease may manifest itself first as ED

Table 3

Vascular ED as a possible early marker of CV disease[5]

Design

- 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, onset of ED preceded CAD symptoms in 67% of patients (99/147)

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other comorbidities and real ED, then one should assess his CV status. This could uncover the patient who is at-risk and provide an opportunity for the FP to discuss with him the positive benefits of lifestyle modification and medications. The patient may not only diminish his risk of future CV disease, but may also reverse or slow the progression of his ED.

It has been shown that we can salvage almost 30% of men whose treatment with oral agents has failed and who are hypogonadal, if we add daily testosterone replacement therapy to their treatment regime.

PED5 inhibitor failures and testosterone

The other concept presented at the MMAS was the consideration for those men that had failed efficacy with PDE5 inhibitors. It is then important to check their testosterone levels. Testosterone is important as an upstream precursor for the development of nitric oxide, as well as accommodating smooth muscle relaxation of the penile blood vessels.

It has been shown that we can salvage almost 30% of men whose treatment with oral agents has failed and who are hypogonadal, if we add daily testosterone replacement therapy to their treatment regime.[3] The addition of testosterone may also help to treat some of the other side-effects of late-onset hypogonadism that we can see in the aging male.

Conclusion

As males age, the prevalence of ED increases while testosterone levels decrease. All of the same risk factors that are implicated in CV disease are also prevalent in those men with ED.

Besides threatening quality of life, ED can also be an early warning sign of impending vascular disease. The primary FP should ask about ED on a regular basis and, if found, should consider a CV work-up. Dx

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