Men’s Sexual Health
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Objectives

- Review prevalence of erectile dysfunction (ED)
- Understand the correlation between diabetes & ED
- Review steps necessary to evaluate patients with ED
- Review ED treatment option beyond Phosphodiesterease type 5 inhibitors (PDE5i)
- Discuss advantages and disadvantages of each therapy for erectile dysfunction
Erectile Dysfunction (ED)

- Inability to maintain an erection form enough for sexual penetration

- 1 in 5 Americans > 20 yrs
- > 39 million American men
- ED increases from 5% to 15% as age increases from 40 to 70 years
- 40% of men effected by age 40, 70% by age 70

Prevalence of Sexual Dysfunction

- Men with poor physical health
- Men with poor mental health
Prevalence of ED in Men with diabetes

- 35-90% of men with diabetes (type 1&2) have ED
- ED occurs 15 years earlier in patients with diabetes
- ED in men with diabetes is more severe and less responsive to oral medications
- In men with diabetes, ED increases with
  - Age
  - Duration of diabetes
  - Poor glycemic control
  - Presence of diabetes complications

J Sex Med 2009;6:1232-1247
Diabetes & Metabolism 2012;30:1-13

Development of Erection

- Complex event involving
  - Psychological
  - Neurological
  - Endocrine
  - Vascular
  - Local anatomical systems
- Process follows the following pattern
  - Stimulation of medical perioptic in the hypothalamus
  - Involve parasympathetic nervous system
  - Nitric oxide
  - Cyclic guanosine monophosphate (cGMP) → arterial inflow
Anatomy of the Male Sex Organ

An erection occurs when blood fills two chambers known as the corpora cavernosa. This causes the penis to expand and stiffen.

Recognizing Risk Factors for ED

- Cardiovascular disease: study reported 49%
  - Hypertension
  - Atherosclerosis
  - Hyperlipidemia
- Diabetes: chronic inflammation ➔ endothelial dysfunction
- Depression
- Alcohol use
- Smoking: decrease production of neural nitric oxide synthase
Neurological Condition That lead to ED

- Cerebral vascular accident (CVA)
- Multiple sclerosis
- Parkinson’s disease
- Spinal chord injury
- Microvascular disease
- Pelvic surgery

Low Testosterone Levels (LTL) as Risk Factor for ED

- Hormone Deficiency (Hypogonadism)
  - 1/3 of the men in one study have hypogonadism
- Frequency in causing ED: LTL < diabetes/vascular disease
- Diminish bioavailability of testosterone
  - Diabetes
  - Obesity
  - Opiate use
  - Thyroid stimulating hormone
  - Gonadotropins
The Challenge of ED in Men with Diabetes

- Hormonal changes
- Functional changes
- Endothelial Dysfunction
- Neuropathy

Other Diseases and Conditions Associated With Erectile Dysfunction

| Cardiovascular causes | *Atherosclerosis  
|                        | *Peripheral vascular disease  
|                        | *Myocardial infarction       |
| Vascular injury        | *Radiation therapy  
|                        | *Prostate cancer treatment  
|                        | *Blood vessel and nerve trauma |
| Systemic diseases      | *COPD  
|                        | *Scleroderma  
|                        | *Renal failure, hyperthyroidism  
|                        | *Liver cirrhosis  
|                        | *Idiopathic hemochromatosis  
|                        | *Cancer and cancer treatment |
| Neurologic causes      | *Epilepsy, Alzheimer disease |
Diseases and Conditions Associated With Erectile Dysfunction (Cont)

| Penile conditions | *Peyronie disease  
|                  | *Epispadias  
|                  | *Priapism |
| Psychiatric conditions |  
|                  | *Performance anxiety  
|                  | *Posttraumatic stress disorder |
| Nutritional states | *Malnutrition |
| Hematologic diseases | *Sickle cell anemia  
|                  | *Leukemias |
| Surgical procedures | *Brain and spinal cord procedures  
|                  | *Retropitoneal or pelvic lymph node dissection  
|                  | *Radical prostatectomy |

Medications and Substances That May Cause or Contribute to Erectile Dysfunction

<table>
<thead>
<tr>
<th>Medication class</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesics</td>
<td>Opiates</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Tricyclic antidepressants</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Phenytoin (Dilantin), phenobarbital</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Lithium, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Dimenhydrinate, diphenhydramine (Benadryl), hydroxyzine (Vistaril), meclizine (Antivert), promethazine (Phenergan)</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>Alpha blockers, beta blockers, clonidine (Catapres), methyldopa, reserpine</td>
</tr>
<tr>
<td>Anti-Parkinson agents</td>
<td>Bromocriptine (Parlodel), levodopa, trihexyphenidyl</td>
</tr>
<tr>
<td>Cardiovascular agents</td>
<td>Digoxin, disopyramide (Norpace), gemfibrozil (Lopid)</td>
</tr>
</tbody>
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<th>Examples</th>
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<tr>
<td>Cytotoxic agents</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Spironolactone (Aldactone), thiazides</td>
</tr>
<tr>
<td>Hormones</td>
<td>5-alpha reductase inhibitors, corticosteroids, estrogens,</td>
</tr>
<tr>
<td></td>
<td>luteinizing hormone-releasing hormone agonists, progesterone</td>
</tr>
<tr>
<td>Illicit drugs</td>
<td>Amphetamines, cocaine, heroin, marijuana</td>
</tr>
<tr>
<td>Immunomodulators</td>
<td>Interferon-alfa</td>
</tr>
<tr>
<td>Antiulcer drugs</td>
<td>Proton proton pump inhibitors [PPIs] and cimetidine</td>
</tr>
<tr>
<td>Lipid-lowering</td>
<td>Statins and fibrates</td>
</tr>
</tbody>
</table>


Diagnosis Algorithm

![Diagnosis Algorithm Diagram]

Comprehensive history

No definable medical Etiology
Consider:
*Screen for psychological causes
*Refer to behavioral therapy
*Review medication history

Definable medical etiology
Maximize treatment:
*Coronary artery disease
*Diabetes
*Hormonal disorders
*Hypertension
*Hypothyroidism
*Neurological conditions

Questionnaire: to categorize ED

Labs: A1c, TSH, AM test. levels

Physical Examination

- Blood pressure
- Peripheral pulses
- Sensation
- Status of the genitalia and prostate
- Size and texture of the testes
- Presence of the epididymis and vas deferens
- Any penile abnormalities, such as hypospadias and Peyronie plaques

Evaluating ED
Sexual Health Inventory for Men (SHIM) Evaluating Experience in the Past 6 Months

(0=no sexual activity/never, 1=very low/ almost never, 2=low/ a few times
3=moderate/sometime, 4=high/most times, 5=very high/ almost always)

- How do you rate your confidence that you could get and keep an erection?
- When you had erections with sexual stimulation, how often were your erections hard enough for penetration?
- During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner?
- During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?
- When you attempted sexual intercourse, how often was it satisfactory for you?
Sexual Health Inventory for Men (SHIM) Evaluating Past 6 Months (Cont)

<table>
<thead>
<tr>
<th>Total Score</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-7</td>
<td>Severe ED</td>
</tr>
<tr>
<td>8-11</td>
<td>Moderate ED</td>
</tr>
<tr>
<td>12-16</td>
<td>Mild to Moderate ED</td>
</tr>
<tr>
<td>17-21</td>
<td>Mild ED</td>
</tr>
</tbody>
</table>


Treatment Pathways for ED

- **First line therapy**
  - Lifestyle modification/mental health consultation
  - Oral therapy with phosphodiesterase type 5 inhibitor (PDE5i) with titration to maximal dose
  - Testosterone supplementation (clinical hypogonadism)

- **Second line**
  - Intraurethral or intracavernosal alprenostil (Carverject)
  - Vacuum pump devices
  - Surgery for erectile dysfunction

Lifestyle Modification

- Quit smoking ➔ improvement of 25% in ED
- Weight loss ➔ 1/3 of men with ED resolution
- Nutritional counseling: Mediterranean diet
- Physical activity
- Decrease alcohol use
- Do not use illicit drugs

Improving ED Through Change in Medication Therapy

- Hypertension
  - Diuretics ➔ calcium channel blockers (diltiazem, amlodipine) may reduce ED
  - Therapy change to Angiotensin Receptor blockers
- Depression
  - Tricyclic antidepressants ➔ bupropion, nefazodone, trazodone

### PDE5i

<table>
<thead>
<tr>
<th>Drug</th>
<th>Standard dose</th>
<th>Recommended time between dosing and intercourse</th>
<th>Onset of action</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sildenafil* (Viagra)</td>
<td>50 to 100 mg</td>
<td>One hour</td>
<td>30-60 minutes</td>
<td>Up to 12 hours</td>
</tr>
<tr>
<td>Tadalafil (Cialis)</td>
<td>10 to 20 mg</td>
<td>30 min</td>
<td>60 to 120 minutes</td>
<td>Up to 36 hours</td>
</tr>
<tr>
<td>Vardenafil* (Levitra)</td>
<td>10 to 20 mg</td>
<td>25-60 min</td>
<td>30-60 minutes</td>
<td>Up to 10 hours</td>
</tr>
<tr>
<td>Avanafil (Stendra)</td>
<td>50-200 mg</td>
<td>30 minutes</td>
<td>15-30 minutes</td>
<td>Up to 6 hours</td>
</tr>
</tbody>
</table>

*High Fat meal reduces efficacy

### PDE5i Side Effects

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side Effects</th>
</tr>
</thead>
</table>
| Sildenafil (Viagra)  | 12%-16%: nasal congestion  
2%-4%: gastric reflux, nausea  
Visual abnormalities  
Typical: Headache, flushing, dyspepsia |
| Tadalafil (Cialis)  | Leg-buttock back pain  
Typical: Headache, flushing, dyspepsia |
| Vardenafil (Levitra) | Leg-buttock pain  
5%-7% priapism  
Typical: Headache, flushing, dyspepsia |
| Avanafil (Stendra)  | Decreased blood pressure  
Typical: Headache, flushing, dyspepsia |

Contraindications to PDE5i

- High cardiovascular risk ➔ use when condition stabilizes
  - Refractory angina
  - Myocardial infarction
  - Uncontrolled hypertension
  - Congestive Heart Failure (NYHA functional classification III/IV)
  - High risk arrhythmias
  - Moderate-severe valvular disease
  - Congenital QT prolongation
- Cerebrovascular accident within 2 week

Medication Interactions Cautions and Contraindications

- Verdafanil ➔ some QT prolongation
  - Quinidine
  - Procainamide
  - Amiodarone
  - Satolol
- Nitroglycerin or nitrate containing compounds
- Caution with alpha blockers due to risk of hypotension
  - ➔ space sildenafil 4 hrs after alpha blocker
  - 25mg of sildenafil ➔ use of alpha blockers is safe
- Dose adjustment in hepatic dysfunction or with medications effecting cytochrome P 450 enzymes
Advantages and Disadvantages of Oral Treatment

- **Advantages of oral drug therapies**
  - Broad patient acceptance
  - Ease of administration and relative efficacy
- **Disadvantages of oral therapies**
  - Contraindications such as the concomitant use of nitrates with respect to PDE5i
  - Relative cost
Other Oral Medications Used for Treatment of ED

- **Vasodilators**
  - Papaverine

- **Dopamine receptor antagonists**
  - Apomorphine SL (sublingual)

- **Adrenergic receptor antagonists**
  - Phentolamine
  - Yohimbine

Natural Therapies for ED Yohimbine

- Component of bark from African tree studies show: improved ED associated with serotonin reuptake inhibitors used in depression
- Adverse effects: increase in blood pressure, irregular heartbeat, anxiety
- Should be used under provider’s supervision

### Natural Therapies for ED

**Dehydroepiandrosterone (DHEA)**

- Increases libido in women
- Helps ED in men
- Product is reported safe in low doses
- Adverse effects: acne

### Natural Therapies for ED

**L-arginine**

- High doses improve ED through stimulation of blood vessels and improvement of blood flow
- Adverse effects: nausea, cramps, diarrhea
- Contraindication: sildenafil

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Natural Therapies for ED
Ginseng

- Study of Panax ginseng shows benefit in ED
- Cream preparation is used for premature ejaculation
- Safe if used on short-term basis
- Adverse effects: insomnia, headache, vertigo


Natural Therapies for ED
Propionyl-L Carnitine

- Combined with sildefanil > sildefanil in ED
- Recommended to be used under medical supervision

Natural Therapies for ED
Ginko

- Potential to increase blood flow to the penis
- Adverse effects: increase the risk of bleeding

Natural Therapies for ED
Horney Goat Weed (Epimedium)

- Substance in leaves of the herb
- Herb not studies in people
- Adverse effects: may effect the heart or breathing functions

Natural Therapies for ED

- Zytenz
- Vigorexin
- Vydexafil
- Magnum
- OxyErect
- Testosym/alpha T1 (claim: testosterone booster)
- Virility EX
- Natural Gain Plus
- ExtenZe
- Happy Ending (claim: improve circulation)

Be Wary of Some Herbal Products

- Herbs contain unknown amounts ingredients
- “Just because the product is natural it does not mean that it is safe” consult with provider
- Review ingredients to prevent potential drug interactions
Androgens

- Benefit in men with low levels of serum testosterone (hypogonadism) <200 ng/dL
- Men with hypogonadism who desire a restoration of libido
- Accomplished with injections, cutaneous application via gel or skin patches, or oral administration (AndroGel, Axiron, Depo-Testosterone, Testopel, Testim, Androderm, Striant, Fortesta)
- Testosterone promotes & maintains secondary sex characteristics in androgen-deficient males


Low-Intensity Shock Wave Therapy” to the Penis (Approved for use in Europe)

- Painless in-office procedure
- Shockwave therapy uses energy from acoustic waves
- Interact with the targeted tissue causing mechanical “micro-trauma”→Triggers the release of growth factors that stimulate the formation of new vessels and more blood flow

Local Therapy

- Alternative to oral therapies
- Medicated Urethral System for Erections (vasodilator)
  - Intracavernosal injection therapy
    - Alprostadil (prostaglandin E1 [PGE1])
  - Intraurethral Therapy
    - Urethral suppository (Muse)
- Vacuum device therapy

Intraurethral Therapy (Muse)

The Medicated Urethral System for Erections (MUSE) is a small suppository placed into the urethra with this device absorbed across the corpus spongiosum.

Alprostadil (Prostaglandin E1)
Smooth muscle dilator of corpus cavernosum

The advantages: less invasive nature
The disadvantages: pain (penis/testes), hypotension, dizziness, partner related vaginal irritation
Injection of Prostaglandin E1 (PGE1; alprostadil) Into One of the Corpora Cavernosa

Advantage: Erection within 5-20 min
Disadvantage: penile fibrosis, pain, injection site hematoma, up to 68% drop out rate

A cross-section of penile anatomy

Additional Side Effects of Alprostadil

- Lightheadness
- Fainting
- Priapism
- Urethral bleeding (intraurethral)
- Penile curvature secondary to scar (intracavernosal)
Vacuum Constriction Devices (VCD)

- Advantages
  - Non-invasive
  - Drug free
  - Cost effective
- Disadvantages
  - Side effects
    - Penile pain
    - Penile numbness
  - Anticoagulants \(\rightarrow\) relative contraindication

VCD apply a negative pressure to the pendulous penis, thus drawing blood into the penis, which is then retained by the application of an elastic band at the base of the penis.

External Erection-Facilitating Devices

- Constricting devices placed at the base of the penis \(\rightarrow\) diminish venous outflow & improve the quality and duration of the erection
- For men who have a venous leak and are only able to obtain partial erections that they are unable to maintain
- These devices may be used in conjunction with
  - Oral agents
  - Injection therapy
  - Vacuum devices
Penile Implants Product Guide

- **Types of penile implants**
  - Non inflatable or semi-rigid penile implants (malleable and non-malleable cylinder rods)
  - 2-piece inflatable penile implants (pump, cylinders)
  - 3-piece inflatable penile implants (pump, cylinders, reservoir)

- **Features of a penile implant**
  - Entirely contained in the body
  - Long-term treatment option
  - Spontaneous
  - Once activated → erection duration as desired by patient

Brands and Models of Penile Implants

- **Non Inflatable / Semi Rigid**
  - Coloplast Genesis
  - AMS 650
  - AMS Spectra
  - AMS Dura II
  - Shah Penile Implant

- **2-Piece inflatable**
  - AMS Ambicor
  - Surgitek PenileImplant Prosthesis

- **3-Piece Inflatable**
  - AMS 700 Series
  - Coloplast Titan OTR/Coloplast Titan
  - Shah Penile Implant

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Coloplast Genesis Flexible Rod Penile Implant (non-Inflatable)

- **Erection**: bending the penis into an erect position
- **Advantage**
  - Simplest of penile implants to surgically implant
  - Long life span → fewer mechanical parts compared to inflatable implants
- **Disadvantage**
  - Infection/pain

AMS Ambicor Penile Implant (Two-Piece Inflatable Model)

- Device consists of
  - Two cylinders in the shaft of the penis
  - A reservoir that holds salt water

How does it work?
- Erection: hydraulic pump to move the salt water from the reservoir to the cylinders→ erection
- Flacid state: Bend the prosthesis down for 6-12 seconds and then release→ valves open→ saline solution to flow back into the reservoir

AMS 700™ Inflatable Penile Implant
(three-piece inflatable penile implant)

• The device consists of
  • Pair of cylinders implanted in the penis
  • A pump implanted in the scrotum
  • A fluid reservoir implanted in the lower abdomen

How does it work?
• Erection: squeezing and releasing the pump moves fluid to the cylinders
• Flacid state: press the deactivation button on the pump


Surgical Implantation
The Final Treatment Option for ED

△ Candidates
  ▪ Patients with vascular insufficiency who failed other therapies
  ▪ Patients who are eligible to receive anesthesia

△ Advantages of penile prosthesis implantation
  ▪ Long lasting effect
  ▪ High patient satisfaction

△ Disadvantages of penile prostheses
  ▪ Irreversibility
  ▪ Invasiveness
  ▪ Surgical complications & prostesis infections (1-5%)
  ▪ Penile deformity & scarring
  ▪ Mechanical failure: <5% in the first yr, 20% at 5 yrs & 50% at 10rs
Percent of Patients Satisfied With Their Treatment

**Percent %**

<table>
<thead>
<tr>
<th>Number of patients satisfied with their treatment</th>
<th>Intracaverinos injection therapy</th>
<th>Oral therapy sildafenil</th>
<th>Penile implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>22</td>
<td>31</td>
<td>32</td>
</tr>
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</table>

**Patient on given therapy**
- 22 Intracaverinos injection therapy
- 31 Oral therapy sildafenil
- 32 patients with penile implants

J Urol 2003;170:159-163

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Pharmacist Impact on ED

- Often the first health care contact regarding ED
- Showed in studies to be highly accurate in ED
- Role in motivating patients to be evaluated by a physician

Pharmacist Role in ED Therapy

- Discuss lifestyle modifications with the patient
- Recommend alternative medication for hypertension/Psychiatric conditions to provider to lessen ED
- Alert the provider to a potential drug interaction with ED therapy
- Refer the patient to a specialist (ex. Nutritionist, psychiatrist)
- Consult the patients on treatment
  - Herbal/OTC
  - Medication adverse effects
  - Proper way to administer oral and injectable products before intercourse

Talk to Your Patient About ED

- Be relaxed, comfortable before you talk to patient
- Don’t’ dismiss fear
  - Men that failed other therapies fear another failed therapy
  - Concern about partner satisfaction
- Remind patients about variety of treatments
  - PDE-5 inhibitors
  - Intraurethral supp/injections
  - Vacuum
  - Surgical implants
- Discuss possibility of implants if other therapies fail
Why is it Important to Talk to Your Patient About ED?

- Discussing ED can help identify hidden issues:
  - Cardiovascular complications
  - Peripheral artery disease
- ED can help motivate many patients to make lifestyle changes
- Resolving ED can help improve partner support
  - Improve communication
  - Resolve feeling of rejection
  - Support lifestyle modifications
- Resolving ED can enhance a patient’s quality of life:

Scenario 1 in ED

- Eric has type 2 diabetes. He takes metformin and basal insulin. His Hemoglobin A1c is 15%. He waits with his wife to pick his prescription. At the counter he becomes angry when Dan (his pharmacist) gives nutritional suggestions relating to diabetes.
- He tells him to direct all of her comments to his wife then says, “It doesn’t matter what I do anymore!” and leaves the pharmacy.
- The wife says that he is upset because he can’t get an erection anymore.
- Dan says, “Speak to his doctor about this. Since good blood sugar control can improve things, let’s finish the discussion of his diet.”
- Do you agree with Dan’s response? What would you do?
L.E.A.P - Listen, Empathize, Affirm, Positively Reframe

- L: “Your husband seems very angry. Tell me more about this. How has it been for you?”
- E: “That has to be difficult for you.”
- A: “ED is very common. The good news is that there are wonderful treatments. Visit edcure.org with your husband to learn more and to see other couples with this issue.
- P: “ED can indicate the start of other issues. Does your husband’s doctor know about this? Would you like me to communicate with the provider?”


Reassessment and Follow-Up

- The need for dose titration or substitution of another treatment intervention
- Patient communication
  - Address concerns regarding treatment administration
  - Address concerns about other sexual dysfunctions (e.g., premature ejaculation), partner issues (e.g., anorgasmia) or lifestyle factors (e.g., emotional stress).
- Monitor adverse drug reactions or drug interactions
- General medical and psychosocial reassessment
- Provides an additional opportunity for patient education
Scenario 2 in ED

Elanor fills Alex’s prescriptions. She meets with Alex to teach him how to inject his basal and bolus insulin dosing. Suddenly, he starts to weep. He says that he must stop his insulin because it makes him “impotent.” He needs to be a real man. Elanor agrees that not being able to perform sexually is a terrible thing, but he must take his insulin or he will develop more health issues. She hands him an insulin injection picture sheet that discusses injection technique and starts to discuss it.

Do you agree with Elanor’s response?

What would you do?

Scenario 2: Managing Alex’s Case

It takes up to 30 min for stress hormone levels to return to baseline* after each “emotional injury.” This is not a time to reason, teach or discuss anything.

L: Tell me more

E: So sorry you are struggling with this

A: You’re not alone. Many men with diabetes develop sexual issues. You have many options. When you feel calmer, we can discuss what to do to help improve the situation.

P: Because you shared your concerns, we can work on making things better for you. Let’s set a time to discuss the different treatment options. There are a lot to choose from.
Counseling and Psychological Care

- Discuss emotional aspects
  - Opening a dialogue allows the clinician to begin the investigation
  - Refer the patient to a consultant (with partner or without)
    - Clarify issues: the couple must work together to resolve the problem
    - Determine which options are beneficial

- Assess man’s confidence
  - Man’s self-esteem and sense of worth
  - Evaluate pure psychogenic ED (normal erections some of the time but is unable to achieve or to maintain a full erection at other times) loses confidence provoke anxiety.

Summary

- Men with diabetes are at higher risk for ED
- Men with ED have many options that can meet their lifestyle
- Role of the pharmacist/healthcare professional
  - Calm the patient and discuss options that the patient has
  - Refer the patient to healthcare professional/mental health
  - Assist in achieving lifestyle modifications
  - Provide information as needed for the provider/patient/family
Resources

- AUA 2018 guidelines
- WWW.EDCURE.ORG
- WWW.ediabetestalk.com

References

5. Diabetes & Metabolism 2012 ;30:1-13
18. J Urol 2003;170:159-163

Questions Please!!!