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# 2018 Canadian Urological Association guideline for Peyronie's disease and congenital penile curvature

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# Disclosures

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**Dr. Bella:** Consultant for Paladin Labs; investigator for Boston Scientific; co-founder and was co-principal investigator for the PROPPER Registry Study

**Dr. Lee:** Advisor for Acerus and Paladin; speaker for Acerus, Astellas, and Paladin; received honoraria from Acerus, Astellas, Paladin, and Pfizer; participant in clinical trials supported by Acerus

**Dr. Grober:** Advisor for Paladin; consultant for Acerus, Apotex, and Mylan; speaker for Acerus and Mylan; holds shares in MHB Labs

**Dr. Carrier:** Advisor for Acerus, Astellas, Boston Scientific, Paladin/Endo, Pfizer, Repros Medical, and Sanofi; speaker for Duchesnay and Janssen; participant in clinical trials supported by Astellas.

**Dr. Brock:** Advisor for Boston Scientific, Eli Lilly, and Paladin; speaker for Astellas, Eli Lilly, Ferring, and Pfizer; hold investments in Eli Lilly and Pfizer; participant in clinical trials supported by Astellas and Ferring



# Background

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1. Burden of disease is significant and PD is often present in otherwise health men
2. Constellation of signs and symptoms – penile deformity (curvature, narrowing, indentation, hinging), erectile dysfunction, penile pain, shortening, and plaque formation
3. Natural history is NOT that of improvement/and or resolution



# Natural history

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1. Plaque-related pain improves and/or resolves in majority of patients even in absence of treatment
2. Conversely, spontaneous resolution or significant improvement or penile deformity is rare



# Relevance

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1. PD prevalence approximated at 5%
2. In clinical practice setting, diagnosis of ED or failed first- and second-line ED treatments warrants ruling out PD
3. Awareness of psychosocial distress has been classically under-represented in the literature and in practice



# Guideline methods

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- Suggestions for management were based on the peer-reviewed literature, the 4th International Consultation on Sexual Medicine (ICSM) (June 2015), International Society for Sexual Medicine Guidelines, American Urological Association (AUA) Guidelines, and Sexual Medicine Society of North America PD management recommendations
- A comprehensive literature search was performed using Pubmed, Cochrane, and EMBASE, with data cutoff at June 30, 2017
- Low quality of evidence in the PD literature made it difficult to make Grade A or B recommendations; the committee did its best to summarize the current literature and provide usable guidance for management



# Diagnosing PD – Patient evaluation

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## Patient evaluation should include:

- History: Onset, duration, history of traumatic event, deformity and erectile changes over time, acquired vs. lifelong, medical history inclusive of family presence of PD, Dupuytren's contracture, other related conditions; prior PD and ED treatments should be documented
- Penile characteristics: Extent of penile deformity, direction of curvature, presence of hourglass deformity, palpable plaque(s), interference with intercourse, penile pain with and without erection, shortening, quality of penile rigidity, presence of hinging
- Sexual function: Erectile rigidity, ability to penetrate, ability to complete intercourse, partner complaints
  - Can use IIEF-5 or PDQ questionnaires



# Diagnosing PD – Physical exam

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- Penis should be examined on the stretch and length determined
- Palpation should be performed to identify the location, size, number, and tenderness of the plaque
- The presence of multiple plaques on both sides of the penis, or plaques within the intracavernosal septum can result in penile shortening with or without deformity



# Diagnosing PD – Physical exam cont'd

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- It is recommended to examine the erection to determine penile length, degree of curvature, hourglass deformities, and rigidity of erection
- Digital photographs at full erection are measured via protractor to determine angle(s) of uni- and multiplanar disease
- Examination after injection of penile injection after vasoactive injection in the office remains the gold standard, especially for the patient reporting complex deformity (hourglass or bidirectional curvature) or ED



# Diagnosing PD – Investigations

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- The most reliable means of assessing deformity is the use of intracavernosal injections, with or without colour duplex ultrasonography
- Combination of ultrasound with ICI may also identify arterial insufficiency or veno-occlusive dysfunction, influencing choice of PD management
- There is no support for the use of high-resolution T2 MRI
- CT and plain radiography also do not have a role routine PD evaluation



# Managing PD

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- Due to the heterogeneity of the disease, PD does not have a clearly defined management pathway
- Patient should be aware that not all urologists have the training, experience, and resources to conduct full evaluation, counsel on various treatment options, and offer care oriented to patient PD and goals



# Non-surgical management

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- As PD does not impact survival, for some men, thoughtful review and counselling regarding impact on QoL, disease course, and management options may constitute “treatment”
- There is no minimum criteria for deformity necessary for management
- The Committee supports a clear discussion with the patient of their PD after evaluation and integration of treatment choices into their care plan



# Oral therapy

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- There is currently no approved oral treatment for PD in Canada
- Vitamin E, tamoxifen, procarbazine, and vitamin E/L-carnitine ARE NOT recommended for standard care of PD
- Oral potassium para-aminobenzoate, colchicine, co-enzyme Q10, and/or pentoxifylline may be considered for use, alone or as a part of multimodal care, but evidence is limited
- PDE-5 inhibitors, specifically tadalafil 5 mg OD, to modify PD plaque progression appear promising, but data is limited to a single published study



# Oral therapy cont'd

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- Oral NSAIDs may be used to control pain associated with inflammation during the active phase of the disease
- The treatment of ED concomitant with PD follows CUA guidelines for the management of ED: oral PDE-5 inhibitors are used in patients for whom there are no medication-specific contraindications
  - If the degree of deformity makes penetrative intercourse difficult, the patient (and partner) should minimize pain and potential injury by limiting positions to those allowing comfortable penetration



# Topical therapy

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- There is potential efficacy with the use of verapamil gel, but current evidence is not strong enough to support its recommendation



# Intralesional therapy

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- Select intralesional therapies can be offered as treatment options for PD
- Advantages include rapid and direct local delivery of the active agent into the target tissue, theoretically without the risk of systemic side effects, and the potential for achieving high local concentrations
- However, most injectable agents used for PD are off-label
- Current data show a lack of standardized outcome measurements, choice of and dose of agent, frequency of delivery, and patient selection criteria to optimize results



# Intralesional therapy cont'd

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- The committee believes that use of intralesional therapy is supported in the literature and clinical experience, and recommends:
  - First-line: clostridial collagenase
  - Second-line: Verapamil or interferon, in cases where cost or concern related to adverse events limits use of collagenase



# Intralesional therapy – Collagenase

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- Two large, multicentre, placebo-controlled, prospective, randomized trials (IMPRESS I & II) have identified optimal patients for this technique of intralesional collagenase with modelling to be: stable disease with a curvature greater than 30° and less than 90°; no isolated hourglass deformity or calcified plaque; and normal erectile function (with or without the use of medications)
- While uncommon, reported adverse events included significant penile hematomas, injection site pain, and penile swelling



# Intralesional therapy – Verapamil

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- 2 decades of Canadian experience
- 11 randomized studies, including 2 RCTs
- Factors – injected volume, frequency, concentration, duration, active vs. chronic phase
- Second-line treatment: cost, concern of adverse events



# Intralesional therapy – Others

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- Intralesional interferon injection: Rarely used in Canada owing to cost and incidence of adverse events
- Corticosteroids: Not recommended for intralesional treatment of PD
- Botulinum toxin A: Has shown a positive response for safety and improvement in penile curvature, but it is too early to make any recommendations



# Intralesional therapy – Others cont'd

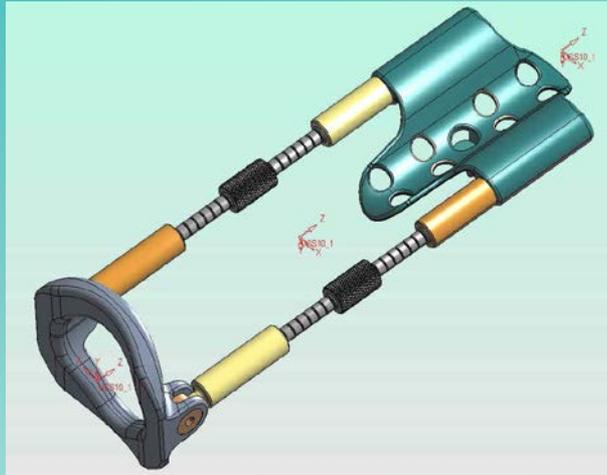
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- There is no Level 1–4 or Grade A–C evidence for platelet-rich plasma (PRP) treatment of PD
- Stem cell treatments for sexual disorders are steadily being introduced into clinical trials and are particularly attractive for PD
  - Clinical applications (safety and efficacy) of this approach are yet to be determined



# Mechanical therapy

- Penile traction is recommended as part of PD management
- It must be noted that all studies vary in the time the devices are applied and the manner in which this is performed
- Additional studies defining the type of device, optimal approach, duration, and tension applied to the penis are needed



# Surgical therapy considerations

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- PD should be stable when surgical intervention is being considered
- General criteria include:
  - Minimum of 6–12 months after disease onset
  - Plaque stability for 3–6 months
  - Deformity precluding or making intercourse difficult
- There are other factors that play a part in a patient's decision-making: failed conservative or medical therapies, extensive penile plaque(s) from the outset, or patient preference for rapid results when disease is stable



# Surgical therapy considerations cont'd

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- It is not incorrect to bypass medical management and proceed straight to surgery; however, the patient must clearly be aware and have consented to the potential treatment side-effects of surgery.
- Although pain is associated with acute phase, if persistent penile pain during erection is related to penile deformity, surgery may be considered even in the presence of said symptom



# Surgical therapy considerations cont'd

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- Managing expectations for PD patients considering surgery is paramount
- Given the psychological impact of PD on the patient, and often his partner, many men have depression or depressive symptoms, decreased self-esteem, and, at times, unattainable expectations in light of factors such as loss of penile length, ED, and sensory changes
- Sensory alteration (decreased penile sensation) is infrequently reported and usually transient in nature, rarely effecting ejaculation and orgasm function



# Surgical therapy considerations cont'd

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- Patients must be made aware of the concept of “functionally straight” (penetrative intromission not compromised, in most cases this corresponds to residual curvature less than  $20^{\circ}$ ) vs. completely straight (comparing to pre-PD anatomy), additional loss of length with tunical shortening approaches, and decreased sexual function (i.e., ED, sensory) with any surgical procedures



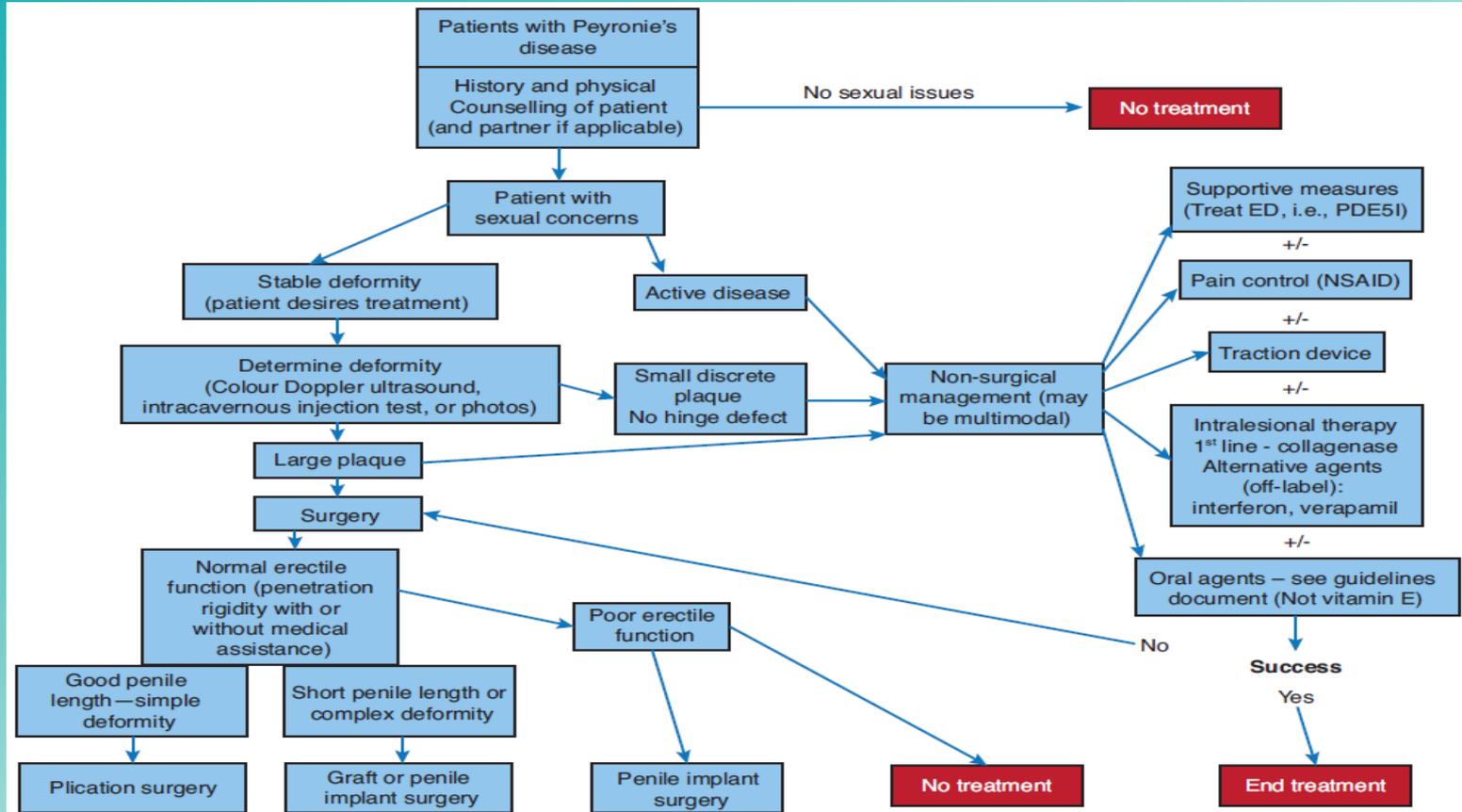
# Surgical therapy considerations cont'd

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- All surgical PD recommendations are considered (Level 3 evidence, Grade C recommendation) based on over 200 observational studies cumulatively published for plication, grafting, and IPP procedures
- There are no RCTs for PD surgery, and interpretation is complicated by design differences, range of inclusion criteria, variance in types of surgery performed and specific outcomes measured, and range of followup durations



# Overview of treatment algorithm



# Congenital penile curvature

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- Disproportionate development of the tunica albuginea of the corporal bodies (not associated with urethral malformation)
- Lifelong curvature, intact erectile function
- Physical curvature interferes with penetration
- Psychological impact on sexual function



# Treatment for congenital penile curvature

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- Treatment is surgical and is offered to patients whose CPC significantly interferes with satisfactory sexual relations of the patient or partner
- There is no role for medical management of the CPC deformity (Level 3 evidence, Grade C recommendation)
- Plication is used almost exclusively, with satisfactory curve correction rates in the order of 67–97%, although there is not a gold standard surgical technique preferred over another, as there remains an absence of comparable outcomes literature



# Conclusion

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- PD burden of disease is significant; non-surgical management is often multimodal
- First-line intralesional therapy with collagenase (Health Canada approved on-label) - see algorithm
- Type of surgical management dependent on PD characteristics and erectile function
- Treatment of CPC is surgical (when required)

