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Transnitrosylation in Nitric Oxide-Mediated Penile Erection

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Nothing to disclose
Nitric oxide (NO) signaling can be mediated not only through cGMP, but also through S-nitrosylation.

**S-nitrosylation**
attachment of an NO molecule to the thiol side chain of cysteine residues to form S-nitrosothiols (SNOs)

Low molecular weight
S-nitroglutathione (GSNO)

GSNOR

GSONH₂
GSSG

S-nitrosylated proteins
To evaluate the role of transnitrosylation in erection physiology and in NO regulation and oxidative stress in the penis using S-nitrosoglutathione reductase (GSNOR)-deficient mice
4-month old male GSNOR-deficient and WT mice

- Erectile function (ICP)

- Molecular studies in the penis
  (protein S-nitrosylation, NO, P-eNOS$^{\text{Ser-1177}}$
  eNOS uncoupling, oxidative stress)
Unexpectedly, electrically-stimulated erectile function is intact in GSNOR^/- mice
- Increased total S-nitrosylated proteins in the GSNOR<sup>−/−</sup> mouse penis
- Decreased NO levels in the GSNOR<sup>−/−</sup> mouse penis
- Denitrosylation is required for shear stress-induced eNOS activation by phosphorylation
- Denitrosylation is required for eNOS coupled function
GSNOR controls oxidative stress in the penis by keeping S-nitrosylation in check
SUMMARY

- Uncontrolled S-nitrosylation decreases NO bioactivity and increases oxidative/nitrosative stress in the penis.

- In the absence of denitrosylation, NO reserves exist (in the form of GSNO), sufficient to produce penile erection, but further insult may predispose to accelerated ED.
Transnitrosylation is a key mechanism of nitric oxide function in the penis through nitrosylation of regulatory proteins, such as eNOS