Kisspeptin-10 — Basic Review Questions

1. What is kisspeptin-10, what type of peptide is it, and what is its regulatory status?

Answer: Kisspeptin-10 is a small peptide — a decapeptide (10 amino acids) — that acts as an agonist at the KISS1R receptor (also called GPR54). It sits at the very top of the reproductive hormone system, serving as the "upstream switch" that turns on the body's reproductive axis. It is given by IV in research and by subcutaneous injection in clinical practice. It is not FDA-approved (investigational only) and has been on the WADA prohibited list since 2024.

2. How does kisspeptin-10 work, and why is acting "upstream" an advantage?

Answer: It works one step above GnRH (gonadotropin-releasing hormone), the brain's master reproductive signal. By binding KISS1R on GnRH neurons, it stimulates them to release GnRH, which drives the pituitary to release LH and FSH, which in turn drive the gonads to make testosterone or estrogen. The defining point is that it stimulates the body's own machinery rather than supplying hormone directly, so the hormone rise is physiological and self-limiting and the axis's normal feedback control stays intact. This "restore rather than replace" approach is its main conceptual advantage over giving exogenous testosterone or a GnRH analog, which override or suppress the body's own axis.

3. What is the human evidence, and how does the response differ between men and women?

Answer: In healthy men, IV kisspeptin-10 reliably and reproducibly raises LH and testosterone and increases LH pulse frequency — this is its best-validated effect. In women, the response is strikingly different and depends on the menstrual cycle: it works well in the preovulatory and luteal phases (and in conditions such as hypothalamic amenorrhea and after menopause) but does essentially nothing in the follicular phase, and it is blunted in women on oral contraceptives. So in women, timing within the cycle determines whether the same dose has any effect.

4. What is the difference between kisspeptin-10 (KP-10) and kisspeptin-54 (KP-54), and why does it matter?

Answer: Kisspeptin-10 is the 10-amino-acid fragment of a longer peptide, kisspeptin-54. They bind the same receptor, but they behave differently: KP-54 lasts longer (about 28 minutes versus about 4 minutes) and crosses the blood-brain barrier, while KP-10 is shorter-acting with limited brain penetration. This matters because much of the strongest reproductive-therapy data — especially using kisspeptin as an IVF trigger — comes from KP-54 and cannot simply be assumed to apply to KP-10.

5. What is the main gap between the evidence and real-world use, and how does that affect dosing?

Answer: The strongest human evidence is intravenous, but real-world clinical practice uses subcutaneous dosing (about 100–200 mcg, several times daily). There is no pharmacokinetic data confirming that subcutaneous KP-10 reaches its target in the brain or reproduces the IV hormone response, and because KP-10 crosses the

blood-brain barrier poorly, whether the subcutaneous route works meaningfully is genuinely unresolved — an honest unknown to disclose. Its very short half-life (about 4 minutes) also means it must be given in frequent, pulsatile doses on cycles (typically 8–12 weeks); continuous or high-dose use causes the response to fade (tachyphylaxis).

6. What other effects does kisspeptin-10 have, and what are the main cautions?

Answer: Beyond reproduction, kisspeptin-10 shows anti-cancer (anti-metastatic), bone-protective, and metabolic effects in laboratory and animal studies, but these are entirely preclinical and should not be assumed to apply to people. The main safety cautions are that it can act as a vasoconstrictor and may promote instability of arterial plaque — so cardiovascular disease is a genuine caution — and that stimulating sex hormones is undesirable in hormone-sensitive cancers (breast, prostate, endometrial). It is also avoided in pregnancy, and all use is investigational and off-label.