Appendix 3

The Frail Proof Protocol

This appendix describes how to prepare and use the 3-part hormone injection (OHPC + estradiol cypionate + testosterone cypionate) for postmenopausal women. The protocol for men and additional information on the protocol for women can be found in the full Frail Proof book. The key to the protocol for women is OHPC (hydroxyprogesterone caproate aka generic Makena), the progestin component. The book has more information on why it, and an all-injection protocol, is superior to all of the alternatives. The other two components are widely used in hormone therapies, with T-cyp being by far the most popular form of T for men on TRT.

There are lots of videos that show how to do subcutaneous (SC/SQ) injections: Search for "insulin injection video". And keep in mind that the average juvenile diabetic learns to self-inject their insulin by the age of 11: If they can do this, surely you can too. Hormones are about as easy to dose as insulin, but it takes slightly more time to draw and inject them: Insulin is water-based whereas these hormones are all dissolved in oil-based carriers. The recommended syringe is commonly known as an "allergy test syringe" (26 gauge 3/8" zero-deadspace), which is smaller and shorter than that used for a flu shot albeit a little larger diameter than typically used for insulin.

You can get E-cyp and T-cyp from most pharmacies, though it will be a special order for many of them. OHPC used to be available from many US-based mail-order compounding pharmacies (e.g., Talon Compounding, Empower, and Vasco Rx) which are generally price competitive with local pharmacies for E-cyp and T-cyp too. But FDA crackdowns on prescribing OHPC for preventing premature birth (for which it is at best marginally effective) have significantly reduced availability in the US in recent years. But it is still widely used and available outside the US and can still be ordered, most commonly as the brand-name product Prolution, from international pharmacies including Inhouse Pharmacy (https://www.inhousepharmacy.vu/) where it is most commonly used for MtF transgender therapy. A more complete list of sources can be found at https://hrtcafe.net/Other_Meds/hydroxyprogesterone.html

If possible get 10ml vials of the hormones with an ethyl oleate carrier. 5ml vials will work, but tend to me more expensive per mg. Other carrier oils will work, but all are thicker than EO (slower to draw and inject) and some (particularly cottonseed and castor) are more likely to cause reactions (usually redness and itching) at the injection site. Unfortunately Prolution uses a castor oil carrier, and is only available in ampoules (glass bottles you must break open), which are less convenient than vials but will work fine in this protocol once you watch a couple of Youtube videos on how to open them. Factory-produced hormones tend to use those two problematic carrier oils, although they'll generally be cheaper than those produced by a compounding pharmacy. It's OK to mix different types of carriers: They'll all blend. The empty sterile vials and syringes are all available on-line at very reasonable prices or from pharmacies, though you may have to accept substitutes from the latter.

The concentrations recommended here are the most common and usually the least expensive per mg. Other concentrations can be used, but the ratio of the components and the dose size will have to be scaled accordingly. Other esters can be used (e.g., testosterone enthanate or estradiol valerate), but again the concentrations will generally be different for those and so the formula will need to be changed to supply equivalent mg per dose. Contrary to standard dosing instructions, these alternative esters are all roughly equally effective and dosing in mg per kg of body weight should be the same. But half-lives matter: For example, E-val has a half-life of 4 days vs. 8 days for E-cyp, so you must inject it at least twice a week and you will end up injecting more (in mg) per week for equivalent effect. Note that even though E-val generally costs less per mg than E-cyp, the fact that you need to inject more and the much greater risk of side effects due to the higher peak values make for a poor cost/benefit tradeoff.

The ratio of the three compounds is 6:4:1 (OHPC:E-cyp:T-cyp. At the concentrations specified below). This recipe makes 11ml, which should last you 12-16 weeks. You can pay to have a compounding pharmacy make this mix for you, but it will be many times more expensive and involve a much longer delay than the $2 and 5 minutes it takes to do it yourself.

The resulting mix has the following concentrations: OHPC 136mg/ml, E-cyp 1.8mg/ml, T-cyp 18mg/ml. A good starting dose for a 120lb woman is 0.8ml of this mix per week, split into two injections (e.g., 0.4ml on Monday morning, 0.4ml on Thursday evening). Dosing should be scaled by body weight. If you're already injecting E-cyp or T-cyp, scale your dose size to match the mg/wk of whichever you're currently receiving. If you know you have particularly low or high

SHBG, you could also take that into account (e.g., increase the dose if your SHBG is over 150, decrease it if it's less than 100). And note that you can easily change the dose size with every shot (unlike, e.g., with pellets where you'd be stuck with an incorrect dose for weeks or months) without risking inadequate endometrial protection because the P:E2 ratio is fixed.

Supplies for producing the mix:

vial of OHPC 250mg/ml
vial of estradiol cypionate 5mg/ml
vial of testosterone cypionate 200mg/ml
empty 10ml sterile vial
5 ml syringe with 17-21 gauge needle
Alcohol prep pad or alcohol-soaked cotton ball

Procedure:

1) Wipe tops of vials with alcohol pad/ball.
2) Draw 5ml of air into syringe with needle.
3) Insert needle into OHPC vial.
4) Push air into vial, and then draw out 6ml of OHPC.
5) Insert needle into empty vial and inject.
6) Draw 5ml of air from the mix bottle to relieve pressure.
7) Repeat steps 2-6 moving 4ml of the E-cyp.
8) Repeat steps 2-6 moving 1ml of the T-cyp.
9) Invert/swirl mix until completely smooth. Don't shake!

If you're using a smaller syringe you'll have to repeat the intermediate steps to move the compounds in multiple steps. If there's not enough hormone left in a source vial, you'll also need to use additional vials to get the right quantity moved into the new vial. Note that vials are usually overfilled, so you can usually get 6ml out of a 5ml vial if you work at it.

Supplies for injecting the mix:

Vial of mix
1ml syringe with 3/8" 26 gauge zero-deadspace needle
Alcohol prep pad or alcohol-soaked cotton ball

Procedure:

1) Swirl mix and check to make sure it's uniform.
2) Wipe top of vial with alcohol pad/ball.
3) Wipe target area of skin with alcohol pad/ball.

4) Draw (dose size) of air into syringe with needle.
5) Insert needle into mix vial.
6) Push air into vial, and draw out (dose size) of mix.
7) Lightly pinch some skin, then push needle in (quickly).
8) Slowly inject contents over several seconds.
9) Wait a second or two for the dose to diffuse.
10) Quickly remove needle.
11) Place (clean) finger (the one used to do alcohol wipe) on injection site and maintain light pressure for a few seconds to prevent leakage and help distribute mix away from injection site.
12) Remove finger and wipe up any leakage, or distribute it and call it "transdermal application", because that's what it is.

You can inject into any area that has a decent fat pad under the skin, but of course you probably also want to use a relatively insensitive location. Most common is to inject into the belly fat or "love handles". The top of the buttocks is also a good choice although it will require having a partner do the actual injecting.

Do labs for E2 (estradiol) and Free Testosterone about a month after starting the protocol, and adjust dosing as required. Target values for E2 are about the average level in premenopausal women (about 100 for Labcorp and Quest: To get a ballpark estimate for other labs, add up the top and bottom of the ranges for the follicular and luteal phases and divide by 4). Free T should be near the top of the lab range (4-5 for Labcorp and Quest). Note that you may have to adjust your ratio if the E2 and T are not off by the same proportion, but you should maintain the 6:4 OHPC:E2 ratio unless a transvaginal ultrasound at 3-6 months shows an endometrial stripe thicker than 5mm which indicates that you need more of a progestin to suppress endometrial proliferation/hyperplasia. Similarly, if you're starting this protocol as the result of failure of a previous protocol (spotting/bleeding or an ultrasound that shows thickened endometrium) using a higher OHPC:E2 ratio may be warranted. The 6:4 ratio is fairly conservative (there should be more P than is necessary for adequate protection) due to the fact that underdosing has far more serious consequences than slightly overdosing and because side effects are rare for OHPC even with doses many times larger than required for postmenopausal hormone therapy (specifically, no sleepiness as is pretty much a standard side effect of OMP (Prometrium) due to the fact that 90% of the latter is metabolized by the digestive system into at least 30 different chemicals that are not progesterone).