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Compounding Pharmacies

Dosage Forms, Vehicles and Methods

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Introduction:
Prior to the proliferation of mega chain drug stores, pharmacies in supermarkets, big box stores, and insurance sponsored mail order companies, all pharmacies were compounding pharmacies. The privately owned pharmacy featured the local pharmacist who was known by name — all of the doctors knew him (in those days, it was almost always a him).

I am the only physician in my family. My father, sister, two uncles and three cousins were pharmacists. I worked summers in my father's drugstore through high school. I remember watching my father and the other pharmacists making up powders, creams, ointments and filling capsules special ordered by physicians. There was regular communication between the local doctor and the pharmacist to make sure everything was right. The compounding pharmacies of today bring back that tradition. The chain stores want their pharmacists to fill as many prescriptions a day as possible. That means just counting out pills or putting a label on a commercially prepared box. There is no time to make or compound anything.

Virtually all human steroid hormones are available from pharmaceutical manufacturing companies. They are packaged as powders and stocked at the compounding pharmacy. All three estrogens, estradiol, estriol and estrone, progesterone, testosterone and DHEA are commonly prescribed. In addition, pregnenolone, melatonin, androstenedione, thyroid hormones T-4 and T-3, as well as freeze-dried pork thyroid are available. Pharmacists also made up many medications for dermatological and veterinary use.

Some compounded products are easier to make than others. Generally, the hormones themselves along with the fillers, creams or gels are not that expensive. The pharmacist's time is the main factor for determining the cost to the customer. Some products (such as creams), may be just as easy to make in a large batch as a small batch. Buying a larger quantity at one time may even save the patient money. These are all good topics for the patient and physician to discuss with their compounding pharmacist.

Type of medication forms available, some of their uses, advantages and disadvantages.

Capsules and tablets:
Any hormone that is effective taken by mouth can also be placed in a capsule. Since the quantities of various hormones are often very small, fillers are used to take up extra space. Some individuals may be allergic or react poorly to some filler types. Sensitive patients should discuss this with the pharmacist. There are several kinds available including milk sugar and cellulose — the filler can be varied depending on patient sensitivity. Commercial products also use fillers but doctors and patients have no choice in how they are made.

Capsules and tablets are easy to take, convenient, travel well and provide consistent, reliable dosage. An oral dosage generally provides more reliable absorption from patient to patient than most other forms. In some cases, if appropriate, several different hormones or medications can be combined into a single capsule in dosage proportions chosen by the physician. This is convenient for the patient and usually saves money. One disadvantage, however, is that the component parts cannot later be varied independently. I usually give separate prescriptions until the dosage is established and stable for the patient. We can later combine the medications for convenience and cost saving. One other minor disadvantage of capsules is that they are quantized. If I decide to raise or lower a dosage, the patient can't take half or three quarters of a capsule, or a little more than one. Tablets can be cut and creams or gels can be used in slightly larger or smaller amounts. Empty capsules come in a variety of colors. This can be used to help patients tell their medications apart. When prescribing capsules or tablets, specify the time of administration, with or without food, and dosage frequency.

There are only a few manufacturers that produce custom-made tablets. One advantage is they can be split for twice a day dosing for the price of one tablet. Belmar Pharmacy in Colorado (belmarpharmacy.com) has been making tablets for many years. Multiple doses may be advantageous when giving estradiol or T-3 (triiodothyronine), both of which can be fairly rapidly metabolized.

All food and medication taken by mouth, passes through the liver after being absorbed in the intestine. This is called the liver first pass effect. Estrogen, for example, has several effects on liver function. On the benefit side, when passed through the liver, estrogen raises good cholesterol (HDL) and lowers bad cholesterol (LDL) On the bad side, that same estrogen raises triglycerides and increases blood-clotting factors. The relative benefits and deficits must be considered when choosing a route of administration.

Oral drops:
In his book about bioidentical hormones, Dr. Uzzi Reiss uses oral drops almost exclusively. He has the patient place a few drops of estrogen or progesterone solution under her tongue for oral absorption. I have had only one patient who was using this method. She frequently had to change her dosage from day to day, and even hour to hour. She was also getting constant hot flashes. I think the main disadvantage is the difficulty of giving a consistent dose. With practice, I am sure the method could be made to work, but other consistent modes of administration are probably superior.

Topical creams:
Most steroid hormones can be administered as topical creams. There are several commercially available formulas. If a patient has an allergy to one type, another can be substituted.

How are topical creams dispensed?
Some pharmacies deliver the creams preloaded into syringes. This makes it easy for the patient to measure out the dose by simply pressing the plunger. Quantities in milliliters are marked on the syringe. Other pharmacies dispense the creams in jars. Cream can be drawn up into a syringe and a measured sample would be used by the patient. I have had patients complain about the difficulty of drawing some creams into a syringe from a jar. Other pharmacies provide small measuring spoons. The pre-filled syringe is the least messy, most accurate and easiest for patients to use. The cost may be higher because many syringes must be provided. Pharmacists use a wide bore needle to fill the syringes from the inside.

Advantages of topical creams: Since the creams are placed topically and diffuse into the bloodstream, the first pass effect is avoided. Another advantage is variability of dosing. If a patient is receiving too much or too little medication, the dose can be adjusted by changing the volume used without having to obtain a entire new prescription. Doses can also be easily divided and used multiple times a day. This patient controlled freedom is a useful feature. Taking multiple capsules a day would also increase the cost.

Disadvantages of topical creams: There is greater variability of absorption with creams than almost any of the other methods. In general, thin-skinned white women seem to have the best absorption while darker skin has the least. It is hard to know if patient application technique, skin type or the cream itself is at fault for poor results. Obtaining blood levels to confirm hormone absorption is a must.

Creams may be messy and take more time to apply than swallowing a tablet or capsule. Since I believe that absorption through the palm is important, this precludes the patient from immediately washing her hands. Also, immediately touching another person might transfer some of the hormone to another individual.

Application for topical creams:
There is some disagreement about the best method and site for application. At some courses that I attended, recommendations were made to apply creams to thin skin areas over a good vascular supple. These areas include the forearm, back of the knee and inside the elbow. Others recommended application to areas with overlying thick layers of fat. They include the thigh and buttocks. In measuring blood levels and asking patients to demonstrate how they exactly apply the creams, I have come to my own conclusion:

It is my belief that the palm of the hand actually is the main site of absorption. I instruct patients to measure out the cream into the palm of their hand and rub vigorously onto another surface such as the opposite forearm or the thigh. Some patients had been placing the cream on one forearm and rubbing with the other

forearm. These women invariably receive very low levels of the prescribed hormones. I do not recommend the forearm-to-forearm technique.

Topical gels:
Topical gels differ from creams in that they usually have an alcohol base. They tend to dry more quickly and are somewhat less messy than creams. Testosterone is absorbed very efficiently using a topical gel. In fact, I find that excess testosterone levels are very easily achieved. The dosage may need to be one-half or even one-fourth of the oral dose. Some physicians have recommended using testosterone directly on the clitoris for sexual enhancement. One must use a vaginal type cream. Alcohol based gels burn if placed on the vulva.

Ointments:
Ointments are vaseline (petroleum jelly) based. They form a barrier against water. When treating vulvar irritation, frequently, urine leakage is part of the problem. Placing the treatment hormones in an ointment protects the vulvar skin from the urine and also prevents washing the treatment hormones away. I sometimes use Colbetasol (Temovate) ointment 0.05% as the base. Estrogen or testosterone can be added by the compounding pharmacist.

Topical liquids:
Some pharmacies make a topical liquid using a base of propylene glycol. The fat-soluble steroid hormone dissolves readily into this liquid and efficiently carried through the skin. Hormones can be dissolved into this base in high concentration — a full day's dose can be carried in a few drops that will rapidly absorb into the skin. The patient can carry a large supply of hormone in a small bottle. There is only one pharmacy in my area that makes this type of preparation and I only have a few patients who have used them. One of my patients was quite happy with this method and normal hormone blood levels were restored. I have some concern with the constant use of propylene glycol, but it is actually an extremely common ingredient in many, if not most, commercial creams and lotions used in the U.S.

Oral troches:
Oral troches are small tablets made to dissolve under the tongue or in the cheek. For patients not successful with creams, using the buccal mucosa is a good alternative to topical skin. Some troches are waxy and dissolve slowly. Others dissolve more quickly. Some pharmacies make small troches and some make them larger, about one centimeter square. To vary the dose, troches are usually soft and can be cut into smaller doses with a knife.

Theoretically troches are absorbed through the skin of the mouth. However, I am sure that much of the dose ends up in the stomach and thereby, the liver. They stimulate the production of much saliva. I am also told that progesterone does not taste very good. Many different flavors can be added as desired. Since progesterone is a sedative, I usually prescribe it before bed. Some patients complain that the waxy troches take up to twenty minutes to dissolve and they end up waiting for their mouth to be empty so they can lie down.

Sublingual tablets:
Sublingual tablets are similar to troches but they dissolve much more rapidly than the waxy troches and are smaller. Not all compounding pharmacies make them.

Vaginal creams:
The base creams used in the vagina are different from the topical vanishing creams. The vagina has an excellent blood supply and all the hormones pass through the vaginal mucosa quiet efficiently. As with the commercial yeast products, there are various plungers and other applicators for measuring and inserting the vaginal creams.

Advantages of vaginal creams: Again, we are avoiding first pass through the liver. In treating vaginal dryness, this places estrogens directly on the tissue with the most need of therapy. There is no wet outer skin to delay getting dressed in the morning.

Disadvantages of vaginal creams: Some women do not like to do vaginal insertion. If the cream is used at night and followed by intercourse, I do not know how much would be absorbed by her partner via the penile skin. I don't think any studies have been done. Also, some women experience increased candida infections when using the vaginal preparations.

Rectal and vaginal suppositories:
In the early 1970s, progesterone vaginal suppositories became popular for PMS treatment. They were made from a cocoa butter base, were messy, and had to be refrigerated. Other bases now exist. Since I use oral progesterone for PMS, I have not ordered vaginal suppositories in years but they should still be efficacious. All of these medications could be used in a rectal suppository, should there be a special reason that other routes of administration could not be utilized.

Pharmacists and doctors are human beings. Sometimes human beings make mistakes. Occasionally I receive a phone call from a patient concerned that a medication they had been using is now causing side effects or is not working. I repeat the laboratory work. I have, on a few occasions, found that patients had estradiol levels over 2,000 pg/ml or testosterone over 500 ng/dl. I assume that the pharmacist made a measurement error. On those few occasions, I had the patient return to the pharmacy to get a new batch. The patient's symptoms returned to normal along with the lab work. The pharmaceutical manufacturers use human error as a reason to avoid compounded medications. I have written thousands of compounded prescriptions. The errors are very rare. The advantages of compounded medications are great. Safety comes in listening to patient complaints and repeating blood test levels.