Menopause 101: Dose, Route, and Formulation

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The history of estrogen as a hormone to treat menopause symptoms is a rich story with many twists and turns. In 1929, estrogen as a hormone was isolated. The first commercial preparation of estrogen was extracted from placental tissue called Emmenin. In 1942, Premarin became commercially available in the US and by 1992 was the number one drug prescribed in the US with sales in excess of $1 Billion by 1997. In July 2002, the release of publications from the Women's Health Initiative (WHI) abruptly changed the landscape altering women's attitudes toward hormone replacement therapy (HRT), now referred to as hormone therapy (HT). This fueled the search for safer delivery systems and formulary options for estrogen. Today, almost all major estrogens are plant or synthesized *de-novo* and are bioidentical. Most estrogens can be delivered via multiple route; oral, transdermal as a patch, spray or gel, and intravaginal ring, cream, insert, in various forms. Different routes of administration will have different metabolic effects. Oral estrogen produces a hepatic first-pass effect not seen with non-oral preparations. Metabolic differences may not translate into clinically significant differences. Ultimately the route of administration is generally determined by patient preference and sometimes cost. Additionally, lowering doses of HT were introduced which reduced risks while maintaining benefits. Consensus statements of several professional organizations were revised to recommend using the lowest effective systemic HT dose for the shortest duration of time to treat vasomotor systems. Improvement in the delivery and understanding of estrogen's role in perimenopausal and postmenopausal women, including risks and benefits, have led to a better quality of life for women as their lifespan continues to increase. With further research and clinical study, this should only continue to improve.