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Hormone Replacement Therapy and Thrombosis Risk: Patient Information

What are blood clots and why are they dangerous?

Blood clots form when the liquid blood solidifies into a 'plug'. This is an important process to stop bleeding and seal over injuries to blood vessels. It can occur in arteries or veins. Unwanted blood clots can sometimes occur for a variety of reasons discussed here. In the veins these are called venous thrombosis and can occur in the deep leg or pelvic veins (**Deep Vein Thrombosis**). Deep vein thromboses can dislodge and travel via the larger veins in the trunk, through the heart and then become lodged in the lung veins. Lung vein clot is called a **pulmonary embolus**. Clots in the lungs are especially serious and large clots can be life-threatening.

What are the risk factors for thrombosis?

There are numerous known risk factors for developing vein clots. These include:

- Overweight or obesity
- Smoking (although this is a lesser risk factor in menopause-related clots it is still a major contributor to other illnesses such as cancer, heart disease and stroke).
- Pregnancy
- Family history of clots
- A genetic tendency to clot (called a thrombophilia)
- A personal history of ever having had a clot in the past
- Surgery, especially major surgery, cancer surgery and bone surgery (orthopaedics)
- Immobility (due to long distance travel, anaesthesia, prolonged bed rest, medical or surgical illness)
- Cancer
- Hormone therapy including the oral contraceptive pill, hormone replacement therapy and hormone treatment for certain cancers
- Inflammatory bowel disease (such as Crohn's Disease or Ulcerative Colitis)
- Severe inflammatory conditions
- Abnormal vein anatomy such as the May Thurner Syndrome
- Increasing age

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Hormone Replacement Therapy and risk of thrombosis (blood clots)

Hormone Replacement Therapy (HRT) is sometimes used to alleviate the symptoms of menopause, when the ovaries stop producing adequate amounts of oestrogen and progrestogen, either due to the natural process of ageing or due to surgical or autoimmune loss of ovarian tissue. HRT can be given as tablets, pessaries, patches or implants. HRT usually contains oestrogen with or without progestogen. As shown above, taking any kind of hormone therapy increases the risk of thrombosis.

Combined oestrogen and progestogen HRT increases the risk of thrombosis about 2-3 -fold

The risk is even higher in women who have had a previous thrombosis.

Compared to women taking a placebo or 'sham' medication, the rate of thrombosis in women taking combined HRT is about 3.5 per 1000 patient years. The risk is highest in the first year of treatment but the risk stays higher than normal for at least 5 years.

What if I take aspirin to thin my blood? Will I be protected?

Aspirin does NOT fully prevent thrombosis in women taking HRT, although there is a small amount of data to say that it may be partially beneficial in clot prevention in these women.

What other clotting risk factors are a problem with HRT?

- Thrombophilias (genetic disorders which predispose people to thrombosis) will multiply the risk of thrombosis in women taking HRT. This is especially true of Factor V Leiden, a common condition in Caucasian women. Women with FVL who also take combined HRT are almost 7 times more likely to have a thrombosis.
- The type of oestrogen is also important, but the data is preliminary and probably not yet strong enough to recommend one oestrogen over another. 'Conjugated oestrogen' carries the highest risk. Esterified (plant derived oestrogen) may have a lower risk.
- Combined oestrogen plus progestogen has a higher risk than oestrogen-alone HRT
- Tibolone may have a lower risk
- The dose of oestrogen is important. The higher the oral dose of oestrogen the higher the risk of thrombosis.
- The route of administration is important. Topical oestrogen such as skin patches carry a much lower risk.

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Summary:

1. There is a small but significant increase in risk of thrombosis in any woman on HRT, but this risk is much higher if other risk factors (listed above) are present.
2. If you are healthy, your absolute risk is likely to be low.
3. Older age, obesity and Factor V Leiden are the strongest additional risk factors for thrombosis in women taking HRT.
4. Smoking, 'statin' anticholesterol medications, and aspirin may not have much effect, either way, on your risk of thrombosis whilst taking HRT.
5. If you have a high risk of thrombosis but your endocrinologist strongly recommends HRT, the risk can be minimised by:
    - Transdermal (patch) oestrogen versus oral (tablet) HRT
    - Optimising your body weight with a healthy diet, strength training and aerobic exercise
    - If recommended by your haematologist, using preventative measures for times of increased risk (such as flights and surgery) to prevent clots. This may include compression stockings or even short term blood thinning medications.

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