Low-molecular-weight heparins have shorter polysaccharide chains and lower molecular weights than unfractionated heparin. Low-molecular-weight heparins are widely used, mainly for thromboprophylaxis. These agents are dalteparin (Fragmin), enoxaparin (Lovenox), certoparin, and a few other less popular preparations. The pharmacokinetic and pharmacodynamic characteristics of LMWHs are substantially different from those of unfractionated heparin.

In clinical practice, LMWHs are much easier and more convenient for patients and physicians to use compared with unfractionated heparin. This is due to their long half-life and few side effects. There is also no need for frequent monitoring of partial thromboplastin time.

Indications during pregnancy

There are several indications for anticoagulation treatment during pregnancy. Pregnancy and the postpartum period are especially thrombogenic. Whenever a condition requiring anticoagulation (eg, a current or recent thromboembolic event) would be treated in non-pregnant patients, it should usually be treated in pregnant patients also.

One exception is thromboprophylaxis for patients with heart-valve prostheses. Several reports, including one from the United States Food and Drug Administration, recommend not using LMWH for these patients during pregnancy. Only heparin should be used (warfarin is teratogenic). Why LMWHs are less effective for patients with this condition is yet to be determined.
**Pregnancy-specific indications**

Antiphospholipid syndrome (APS) is associated with adverse pregnancy outcomes. A few controlled trials suggest that a combination of heparin and acetylsalicylic acid improves pregnancy outcomes in women with APS.\(^2\),\(^3\)

In recent years, many reports have found an association between various thrombophilias and adverse pregnancy outcomes, such as preeclampsia, abruptio placentae, intrauterine growth restriction, recurrent abortions, and fetal death.\(^4\)-\(^7\) Only very limited hard data support use of LMWH for women with previous adverse pregnancy outcomes and thrombophilias. Nevertheless, offering these women anticoagulation therapy is relatively common. A recent article\(^8\) has suggested that, for women with previous pregnancy loss and thrombophilia (namely factor V Leiden and prothrombin mutation), administration of LMWH rather than ASA improves pregnancy outcome. This new report might further increase use of LMWHs for women who have had previous adverse pregnancy outcomes.

**Dosage and monitoring**

In various reports, doses of dalteparin ranged from 2500 to 22000 units in one or two subcutaneous (SC) injections daily. For enoxaparin, doses ranged from 20 mg/d to 120 mg/d divided into one or two SC injections daily.

There is no way of comparing dosage equivalences among the various LMWHs unit by unit, by pharmacokinetics, or by bioactivity. Testing anti-Xa levels will allow physicians to monitor LMWH levels 3 to 4 hours after administration. The importance and optimal frequency of monitoring anti-Xa levels during treatment with LMWH are still debatable.

**Side effects**

The most common side effects of heparin are bleeding, osteoporosis, and heparin-induced thrombocytopenia. The LMWHs have weaker interactions with platelets and inhibit bone formation less than unfractionated heparin. They also have higher bioavailability after SC administration, have a longer half-life, and are less bound to plasma proteins. All these factors make LMWHs less likely than heparin to cause side effects. Much less osteoporosis is seen with LMWH treatment. One recent study showed no difference in bone density until after pregnancy between women who had and had not been treated with LMWHs.\(^9\),\(^10\) Heparin-induced thrombocytopenia is very rare with use of LMWH.

A common side effect reported is skin irritation at the injection site. This should not result in cessation of treatment.

**Transfer to fetus and milk**

An in vitro experimental study by Motherisk showed that LMWHs did not cross the placenta.\(^11\) A clinical report, where LMWH was injected shortly before a late pregnancy termination, showed that anti-Xa was detected in the women but not in the fetuses, indicating no LMWH crossed the placenta.\(^12\) In retrospective studies, no specific adverse fetal effects or teratogenicity were detected.\(^13\) It should be noted that LMWHs are classified by the Food and Drug Administration as pregnancy category B (no evidence of adverse effects on humans). The concentration of LMWH in maternal milk was very low.
low, more than 10 times lower than in maternal serum, and thus had no clinical significance. Women treated with LMWHs can safely breastfeed.

References