

# RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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## Antithrombin deficiency

Antithrombin III (ATIII) is a glycoprotein that circulates in human plasma, and can inactivate thrombin and other proteases of the clotting cascade. Deficiency in ATIII leads to an increased risk of thrombus formation, due to prolongation of the circulation of activated clotting factors. The condition may be either inherited or acquired.

Inherited ATIII deficiency is classified into two types. Type 1 ATIII deficiency is associated with genetic mutations that lead to reduced production of the antithrombin protein. If the condition is homozygous it is usually fatal *in utero*. In type 2 ATIII deficiency, the antithrombin protein is still produced and secreted, but may have abnormalities associated with its structure. This is not usually associated with high risk of thrombosis, unless the condition is homozygous.

The morbidity associated with the condition varies widely depending on the level of functional antithrombin. It is thought that levels below approximately 50% of normal are associated with an increased risk for thrombotic complications. Patients usually present from twenty years of age with a deep vein thrombosis or pulmonary embolus, however some patients will not be affected until a precipitating event occurs, such as pregnancy, trauma, or the commencement of medication such as the oral contraceptive pill.

Patients with known ATIII deficiency should receive lifelong treatment with an anticoagulant. For the prevention and treatment of thrombosis and pulmonary embolism, during surgery, pregnancy and child birth, a preparation of human ATIII (Thrombotrol-VF), is most commonly prescribed. The TGA has approved Thrombotrol-VF for use in patients with hereditary deficiency of ATIII. It is prepared with human plasma from voluntary donors. Small clinical trials have shown efficacy of the product as treatment or prophylaxis in both acquired and inherited conditions. Initial dosing is based on the equation below, but it should be adjusted on an individual basis:

$$\frac{(\text{Desired} - \text{pretreatment ATIII level}) \times \text{weight}}{2.2}$$

ATIII levels should be determined pre-treatment, at 20 minutes, and then as a pre-dose trough, prior to subsequent infusions, in order to adjust dosing to maintain ATIII levels at greater than 80% of the normal level.

Management of an acute thrombotic event is determined by the patient's response to heparin, which will depend on the level of antithrombin produced by the liver. In many cases ATIII concentrate will also be required.

Recently, the US FDA approved a recombinant human antithrombin (ATryn) for use in patients with congenital ATIII deficiency in high risk situations for thrombosis. This therapy may be more acceptable in the future as it is not a blood derived product.

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**FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: [chris.alderman@rgh.sa.gov.au](mailto:chris.alderman@rgh.sa.gov.au)**  
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