time are extensively used as indicators of platelet function. Nevertheless, the following laboratory tests are commonly performed to further determine detailed changes in platelet activation.

Tests of platelet secretion

The specific α-granule contents can be determined in plasma and are indices of in vivo platelet secretion. The granule contents include platelet factor 4, β-thromboglobulin, soluble P-selectin, and thromboxane A2 (TXA_2) metabolites. In recent years, these plasma assays have seldom been used to evaluate platelet function due to their poor specificity.

Platelet aggregation tests

Platelets in blood, in plasma, or as an isolated cell population do not interact with one another. If an appropriate agonist is added to the cells, however, rapid aggregation of platelets can ensue. A platelet aggregometer is a modified spectrophotometer which measures changes in light transmission through a platelet preparation. The maximal height of the aggregation trace is measured as an indicator of the aggregation response. The common platelet-aggregating agonists include adenosine diphosphate (ADP), epinephrine, arachidonic acid, collagen, and thrombin.[2]

Studies of platelet activation

Monoclonal antibodies (MoAbs) can be used in a flow cytometric assay to measure the expression of any platelet surface antigen. Some antibodies bind specifically to activated platelets but not to resting platelets. Among these activation-dependent MoAbs, the 2 most widely studied are those directed against conformational changes in the GPIIb-IIIa complex and those directed against granule membrane proteins. Using this technique, investigators can rapidly and accurately measure activated platelets.[3]

Measurements of intermediates in platelet signal transduction

The signaling pathway of platelet activation has been well studied.[4] Platelet-aggregating agonists bind to heptahelical receptors coupled to heterotrimeric G proteins in the platelet membrane. The consequence is activation of the phospholipase C-β subunit (PLCβ) by the activated α subunit of Gq, resulting in hydrolysis of phosphatidylinositol 4,5-bisphosphate (PIP_2) and production of the second messengers, inositol 1,4,5-trisphopsphate (IP_3) and diacylglycerol (DAG). IP_3 then promotes calcium release from intracellular stores. Every intermediate in the cascade can be measured to elucidate the mechanism of platelet activation.

VOLATILE ANESTHETICS

In the current clinical practice of anesthesia, there are 5 volatile anesthetics commonly used: halothane, enflurane, isoflurane, desflurane, and sevoflurane. Among these, the effect of halothane on platelet function has been studied most thoroughly. The effect of halothane on platelet aggregation has been investigated using platelet aggregometry in vitro (Table 1).[5-12] Bjoraker[6] reported an insignificant effect of 2% halothane on platelet aggregation, but the design of that study was criticized for using 50 μM ADP as an agonist for platelet stimulation, which is 5 to 50 times greater than the concentration used by most investigators and which could mask the effect of halothane on platelet aggregation. Most other authors agreed that in vitro platelet aggregation would be inhibited by halothane at clinically used concentrations. On the other hand, several in vivo studies revealed conflicting results about the inhibitory effect of halothane (Table 2).[13-18] In these in vivo studies, patients undergoing surgical procedures received general anesthesia with halothane, and their blood was drawn and evaluated by platelet aggregometry. In some studies, bleeding time was also measured using a template device. Different results of these intraoperative studies occurred due to differences in methodology. For example, if a blood sample is not sealed tightly, the volatile agents will evaporate out of the blood sample prior to analysis. This might explain the different results from Lichtenfeld et al..[15] Other studies all reported that halothane at clinical concentrations had inhibitory effects on platelet aggregation. At present, most scientists accept the concept that halothane has an inhibitory effect on platelet aggregation both in vitro and in vivo.

The relationship between halothane and platelet function was also investigated in animal models. In 1983, Cambria et al.[19] used γ-imaging to examine platelet deposition on polytetrafluoroethylene arterial grafts in dogs and they found that halothane decreased