

Platelet Testing Guidelines

July, 1981

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(Retyped 10/6/92)

## Platelet Testing Guidelines

Significant procedural or equipment changes in collection, processing or storage of platelets necessitate evaluation of platelet function. In the past, the Bureau has required bleeding time studies as the definitive demonstration of platelet efficacy. Such studies are difficult to organize and perform, and we believe that the limited number of investigators available to perform these studies may seriously delay testing and approval of new procedures and equipment

The difficulty inherent in testing platelets in the laboratory has been described in many publications. A few of these conclude that clinical behavior and laboratory testing cannot be correlated. The Bureau does not subscribe to this extreme view, on the basis of extensive input from workshops and advisory meetings. We believe that the complexities of laboratory platelet testing need not interdict its use in the evaluation of platelets for transfusion. However, the limitation of various tests must be clearly understood.

We suggest that testing protocols be designed in three stages:

- I. Evaluation of functional integrity.
- II. Evaluation of survival in the circulation.
- III. Evaluation of clinical hemostatic efficacy.

## I. Functional Integrity

The purpose of this phase of testing is to demonstrate that the platelets under investigation behave similarly to platelets treated by accepted methods. There are many published procedures for testing platelets. The correlation between such tests on stored platelets and the clinical efficacy of the platelets is an unsettled question. Since many potentially valid methods exist, and since most laboratories use only a small number, we will not require any specific group of tests. Rather, we suggest that the following general approach be used:

1. Measurements should focus on platelet morphology (especially by transmission electron microscopy) and on the basic physiologic reactions, namely shape change, release and aggregation. Clot retraction does not correlate well with whole cell viability and is not recommended.

The following tests have been found helpful by some workers:

(References are listed as examples of pertinent work)

### A. Serotonin uptake

(Hardemann, MR & Heynens, CJL:

Thromb. Diath. Haemorrh. 32:405, 1974

### B. Resistance to hypotonic stress.

Valeri, et al. Transfusion 14:331, 1974)

### C. Estimation of discoid morphology by

light microscopy (Kunicki, TJ et al.,

Transfusion 15:414, 1975), or by light

transmission (Dohme, 8 & Murphy,  
S. J. Lab. Clin. Med. 92:53, 1978)

D. Electron microscopic evaluation of morphology.

(White, JC. Ultrastructural Physiology and Cytochemistry of Blood Platelets, in, The Platelet ed. by Brinkhous, KM, Shermer, RW and Mostofi, FK, 1971, Williams & Wilkins, p.83.

E. Measurement of aggregation or release response to a series of concentrations of one or more agonists (dose-response studies). Platelet reactivity after storage should be compared with reactivity of fresh platelets, or of platelets prepared and stored with accepted methods.

(See, for example, White, GC et al, Transfusion 19:411, 1979).

F. Measurement of cellular ATP, or of the adenylate energy charge. (Akkerman, JWN. Thromb. Haemost. 39:712, 1978).

The above are listed as illustrations and investigators will not be restricted to these.

2. The stimuli chosen should be those best suited to the experimental system employed (e.g., thrombin may not be suitable in a plasma system and some ionophores may not yield physiologically valid data).

3. Since stored platelets will be transfused, the test conditions should mimic the conditions to be expected within a recipient (by use of either normal plasma or a substitute as a final suspending medium).

## II. Platelet Survival

Changes in platelet structures may affect ability to circulate without a concomitant change in laboratory behavior. Autologous recovery and survival should be studied in normal persons, using a reliable and reproducible marker. Most laboratories will choose radioactive labeling. A sufficient number of donors should be studied to clearly demonstrate satisfactory results. This number will be determined by the variety of storage conditions to be tested and by the degree of scatter in the data such studies will require that an IND application be filed and approved.

## III. Clinical Hemostatic Efficacy

We believe that platelets which are proven satisfactory in stages I and II of testing will be clinically functional. Said another way, we do know of any characterized platelet defect, natural or induced, which would fail to be detected by the approach described above. Thus, when such testing is completed, evaluation under actual clinical use conditions remains as the final step.

Clinical performance should be assessed by introducing the test platelets into the regimen of platelet transfusions given to patients. In way, test platelets can be compared to platelets prepared by accepted techniques. The observations made should relate to the patient's hemostatic function, should be described in a protocol as part of the IND application, and may include any clinical measurements (e.g., epistaxis, hematuria, petechiae). Pre- and post-transfusion platelet counts will be an important component of these data. Bleeding time studies are not required, but may be submitted as the stage III testing.

Since this phase of testing is designed to determine whether the technique can be used under actual clinical conditions, the protocol should describe use of more than one blood establishment and a reasonable number of patients.

The Bureau believes that this approach to platelet testing will expedite approval of new technologies. The testing required is specialized, but is available at many institutions.