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Standard Practice for Assessment of Hemolysis in Continuous Flow Blood Pumps[1]

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INTRODUCTION

The goal of blood pump development is to replace or supplement the function of the human heart. As a result, continuous flow blood pumps, including roller pumps and centrifugal pumps, are commonly used in clinical extracorporeal circulation. They are used not only for cardiopulmonary bypass in routine cardiac surgery but also for ventricular assist, percutaneous cardiopulmonary support, and extracorporeal membrane oxygenation.

Many investigators have attempted to develop an atraumatic blood pump. Hemolysis is one of the most important parameters of blood trauma induced by blood pumps. However, comparative *in vitro* evaluation of the reported results of hemolysis are difficult due to the lack of uniformity of the test methods employed. Thus, it is necessary to standardize the method of performing *in vitro* hemolysis tests for the evaluation of continuous flow blood pumps.

1. Scope

1.1 This practice covers a protocol for the assessment of the hemolytic properties of continuous flow blood pumps used in extracorporeal or implantable circulatory assist. An assessment is made based on the pump's effects on the erythrocytes over a certain period of time. For this assessment, a recirculation test is performed with a pump for 6 h.

1.2 The values stated in either SI units or inch-pound units are to be regarded separately as standard. The values stated in each system may not be exact equivalents; therefore, each system shall be used independently of the other. Combining values from the two systems may result in non-conformance with the standard.

1.3 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

1.4 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

F1830 Practice for Selection of Blood for ***in vitro*** Evaluation of Blood Pumps

3. Terminology

3.1 *Definitions:*

3.1.1 *continuous flow blood pump*—a blood pump that produces continuous blood flow due to its rotary motion.

3.1.2 *free plasma hemoglobin*—the amount of hemoglobin (iron or heme-containing protein) in plasma.

3.1.3 *hemolysis*—damage to erythrocytes resulting in the liberation of hemoglobin into the plasma.

3.1.4 *Index of Hemolysis*

3.1.4.1 *normalized index of hemolysis*—added grams of plasma free hemoglobin per 100 L of blood pumped, corrected for plasma volume using hematocrit and normalized by flow rate and circulation time.

3.1.4.2 *normalized milligram index of hemolysis*—normalized index of hemolysis expressed by milligram value of free plasma hemoglobin.

[1] This practice is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.30 onCardiovascular Standards.

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[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

3.1.4.3 *modified index of hemolysis*—mass of hemoglobin released into plasma normalized by the total amount of hemoglobin pumped through the loop.

4. Formulas

4.1 *Normalized Index of Hemolysis (N.I.H.)* (**1**, **2**, **3**, **4**)[3]:

$$N.I.H.\ g/100l = \Delta freeHb \times V \times \frac{100 - Ht}{100} \times \frac{100}{Q \times T} \quad (1)$$

Δfree Hb = increase of plasma free hemoglobin concentration (g/L) over the sampling time interval,

where:

V = circuit volume (L),
Q = flow rate (L/min),
Ht = hematocrit (%), and
T = sampling time interval (min).

4.2 *Normalized Milligram Index of Hemolysis. (mg.N.I.H.)* (**2**, **3**, **4**):

$$-mg.N.I.H.mg/100l = \Delta freeHb \times V \times \frac{100 - Ht}{100} \times \frac{100}{Q \times T} \quad (2)$$

4.3 *Modified Index of Hemolysis (M.I.H.):*

4.3.1 Modified index of hemolysis (M.I.H.) (**5**, **6**) that can be written with no units or as (milligram of hemoglobin released into plasma/mg of total hemoglobin pumped through the loop):

$$M.I.H. = \Delta freeHb \times V \times \frac{100 - Ht}{100} \times \frac{10^6}{Q \times T \times Hb} \quad (3)$$

where:

Hb = total blood hemoglobin concentration at time zero (mg/L), and
Δfree Hb = increase of plasma free hemoglobin concentration (mg/L) over the sampling time interval.

4.3.2 Among these indices, M.I.H. is recommended as an index to express the degree of hemolysis caused by a blood pump in a recirculating system. N.I.H. was proposed to account for the plasma volume based on the hemotocrit. Recent development of less hemolytic blood pumps has since made it convenient to use mg. N.I.H. rather than N.I.H. However, both the N.I.H. and the mg N.I.H. vary with hematocrit of the blood (**6**). M.I.H. is the recommended index to express the degree of hemolysis caused by a blood pump in a recirculating system. The M.I.H. equation corrects for differences in blood hemoglobin concentration and hematocrit directly (**5**).

4.4 *Testing Blood*—Because the level of trauma-induced hemolysis is different based on the source of blood, it is necessary to identify the source of blood and its respective index of hemolysis. Human, bovine, or porcine blood are recommended as the primary sources of testing blood (see Practice F1830). It is preferable that the blood collected at a standard slaughter house not be used due to the risk of being contaminated with fluids other than blood, unless the blood is obtained by controlled venipuncture. Although animal blood is used in the development stage of a pump, it is suggested that pre-clinical evaluation tests be repeated with human blood.

5. Summary of Practice

5.1 *Blood*—The blood is obtained from human volunteers, cattle or pigs having normal body temperatures, no physical signs of disease, including diarrhea or rhinorrhea, and an acceptable range of hemotological profiles. The blood should be collected by vascular puncture using a needle (14G or larger) and collected into the standard 500–2000 mL bags containing citrate phospate dextrose adenine (CPDA-1) anticoagulant solution (See Appendix X2) or heparin sulfate (See Appendix X3). The blood from a slaughterhouse can typically be used if it is obtained by controlled venipuncture.

5.2 *Test Loop* (**4**) *(See Fig. 1)*—The test loop consists of a total of 6.6 ft [2 m] of 3/8 in. [9.5 mm] ID polyvinylchloride tubing and a reservoir (typically, 13 by 13 cm) with a sampling port. The primed blood volume is 450 ± 45 mL. A screw clamp, that is positioned at the outlet side, is applied to produce the required conditions for the left heart assist application (5 L/min against 100 mm Hg pressure head (that is, with the pressure sampling ports at the same vertical height, the pressure in the outlet line of the pump is 100 mm Hg greater than in the inlet line)) and for the cardiopulmonary bypass application (5 L/min against 500 mm Hg pressure head). (Optional testing at 350 or 700 mm Hg is also advisable.) To monitor such pressure heads, the pressure monitoring lines are incorporated into the test loop both at the inlet and outlet tubes. An ultrasonic or electromagnetic flow probe is placed at the outlet side of the pump between the clamp and the reservoir to monitor the flow rate. A thermistor is connected to the loop, and the blood temperature is measured using a corresponding thermometer.

5.3 *Pump Conditions*—Pump flow rate is set at 5 ± 0.25 L/min at the circulating blood temperature of 37 ± 1°C. The total pressure head is set at 100 ± 3 mm Hg for the left heart assist application and 500 ± 15 mm Hg for cardiopulmonary bypass application. However, additional testing temperatures can be chosen from 0 to 42°C according to the intended clinical use of the pump (for example, cardiopulmonary bypass may include cooling and warming during surgery.)

5.4 *Evaluation*—The free plasma hemoglobin is determined by a clinically approved assay method (see 9.3). The free plasma hemoglobin is standardized by calculating the M.I.H.

6. Significance and Use

6.1 The objective of this practice is to standardize the evaluation method for detecting the hemolytic effect of a continuous flow blood pump used in extracorporeal circulation and circulatory assistance.

7. Preparation of Hemolysis Test

7.1 *Blood*—The blood is obtained from human volunteers having normal body temperature, exhibiting no physical signs of disease and having hematological profiles in the normal acceptable range. (Donors are subjected to standard blood donor screening procedures.) The donor should be fasted for 8

[3] The boldface numbers given in parentheses refer to a list of references at the end of the text.