Platelet Interactions with Dacron Vascular Grafts

A Model of Acute Thrombosis in Baboons

Stephen R. Hanson, Herculaas F. Kotze, Brian Savage, and Laurence A. Harker

We have developed a model of acute Dacron graft thrombosis in baboons in order to assess platelet alterations secondary to arterial thrombus formation. In this model, thrombus formation was initiated by Dacron vascular grafts inserted as extension segments into chronic arteriovenous Silastic shunts. Following platelet labeling with $^{111}$In-oxine, platelet deposition was measured for 1 hour following blood contact under arterial flow conditions using a scintillation camera. Graft platelet activity rapidly increased 40- to 50-fold, plateauing by 1 hour. All grafts produced equivalent reductions in circulating platelet count and blood $^{111}$In-platelet radioactivity, demonstrating that the labeled cells were functionally equivalent to the total platelet population. After graft placement, the remaining platelets survived normally. Acute platelet deposition was equivalent on grafts placed 1, 24, 48, and 72 hours following injection of the labeled cells, indicating that a variable delay between platelet labeling and graft imaging was without detectable consequence. Platelet destruction by the graft produced a tenfold increase in plasma levels of platelet factor 4 (PF4) and $\beta$-thromboglobulin (BTG) but did not modify either the $\alpha$-granule (PF4, $\alpha$TG) or dense granule (ADP, ATP) contents of circulating platelets.

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We have studied the hemostatic mechanism in the baboon and found it to resemble closely that of humans in a number of respects, including concentrations of coagulation factors and plasminogen, bleeding time, platelet count, platelet volume, platelet morphology, platelet aggregation and release in vitro, and plasma levels of platelet factor 4, beta thromboglobulin, and fibrinopeptide A using human radioimmune assays (unpublished observations).

**Methods**

**Animals**

We studied 14 normal male baboons (Papio anubis) weighing 8 to 14 kg who had been dewormed and observed to be disease-free for at least 6 weeks prior to use. Circulating platelet concentrations averaged 380,000 ± 91,000 platelets/μl (± 1 sd), and white cell counts averaged 8300/μl ± 4100. All animals had a chronic arteriovenous shunt surgically implanted between the femoral artery and vein. We have studied the hemostatic mechanism in the baboon and found it to resemble closely that of humans in a number of respects, including concentrations of coagulation factors and plasminogen, bleeding time, platelet count, platelet volume, platelet morphology, platelet aggregation and release in vitro, and plasma levels of platelet factor 4, beta thromboglobulin, and fibrinopeptide A using human radioimmune assays (unpublished observations).

**Vascular Grafts**

Uncrimped knitted Dacron grafts (Sauvage external velour, mean porosity 2000 to 2200 ml/H₂O/min at 120 mm Hg) were a gift from Roger Snyder, U.S. Catheter, Incorporated, Billerica, Massachusetts. All grafts were 10 cm in length, 4.0 mm i.d. Prior to evaluation in the arteriovenous shunt system, the grafts were rendered impervious to blood leakage in the following manner. First, a 4.0-mm Teflon rod (that had been thoroughly cleaned using a mild soap solution, then ethanol, and finally by rinsing with sterilized distilled water) was inserted through the graft. The graft was then externally wrapped with a 5 × 10 cm sheet of Paraflm (American Can Company, New York, New York) and placed inside a 10-cm length of 6.3-mm i.d. "heat shrink" Teflon tubing (Small Parts Incorporated, Miami, Florida). The Teflon tubing containing the graft segment was gently heated over a low Bunsen flame until shrinkage to about 5.3 mm had occurred, resulting in a compression of the Paraflm onto the external fabric interstices without modification of the luminal graft surface as documented by scanning electron microscopy (data not shown). Silicone rubber tubing, 10 cm × 4.0 mm i.d., was transferred onto the Teflon rod and connected to both ends of the graft segment with Silastic Medical Adhesive (Type A, Dow Corning Incorporated). When the polymer had cured for 24 hours, the Teflon rod was carefully pulled from the tubing lumen (Figure 1). This procedure produced impervious grafts rigidly constrained to a linear geometry, and having an inner diameter of precise dimensions (4.0 mm). The resulting flow channel was smooth in its transition from the Silastic to the graft without imperfections due to the coupling procedure.

The 4.0-mm i.d. Silastic tubing segments proximal and distal to the Dacron graft were connected to the 3.0-mm i.d. Silastic tubing comprising the chronic arteriovenous shunt with 2-cm long tapered Teflon connectors (Small Parts, Incorporated).

Mean blood flow rates through vascular graft segments incorporated into the A-V shunt system were measured continuously using a Doppler ultrasonic flowmeter (L and M Electronics, Daly City, California) and "C" shell cuff type transducer probe which fitted snugly around the Silastic tubing comprising the chronic shunt. The flowmeter and probe were calibrated in vitro using whole baboon blood. In all studies initial blood flow rates ranged from 170 to 220 ml/min.

Following 60 minutes exposure to flowing blood, vascular graft segments were removed and perfused with 2.5% glutaraldehyde in 0.1 M phosphate buffered saline, pH 7.4. All grafts were perfused at a rate of 100 ml/min for 5 minutes. Graft segments were subsequently dehydrated in increasing concentrations of ethanol, critical point dried, and sputter-coated with approximately 35 nm of gold-palladium for scanning electron microscopy.

![Figure 1. Dacron vascular graft connected to silicone rubber tubing. After removal of the Teflon rod, a smooth flow channel is achieved.](image-url)
Laboratory Procedures

Autologous baboon blood platelets were labeled with \(^{111}\text{In}\)-oxine according to the following protocol. Whole blood (100 ml) was collected directly into plastic bags (TA-3, Fenwal Labs, Deerfield, Illinois) containing 20 ml acid-citrate-dextrose anticoagulant (NIH formula A). The blood was centrifuged in the bag at 300 g for 10 minutes. The supernatant platelet-rich plasma (PRP) was transferred to a second bag and pH adjusted to 6.5 by the addition of 0.15 M citric acid (0.1 ml/10 ml PRP). The red blood cell fraction was returned to the donor animal. The platelets were formed into a pellet by centrifugation of the PRP at 1300 g for 15 minutes. The supernatant platelet-poor plasma (PPP) was completely decanted and discarded. To remove residual plasma proteins, the bag containing the platelet pellet was carefully washed once by overlaying with 30 ml of Ringer’s citrate dextrose (RCD; pH 6.5) which was then decanted and discarded. The pellet was then gently resuspended in 5.0 ml RCD, and incubated for 30 minutes with 500 to 700 \(\mu\text{Ci}^{111}\text{In}\)-oxine (Amersham Corporation, Arlington Heights, Illinois). Contaminating red cells were removed by a final slow centrifugation at 200 g for 5 minutes. Labeling efficiency was determined by diluting 200 \(\mu\text{l}\) of the labeled-platelet concentrate with 5.0 ml RCD, and comparing the activity in 0.5 ml of the diluted platelet suspension with the activity in 0.5 ml of cell-free supernatant following centrifugation at 3000 g for 30 minutes. In the 14 studies involving platelet labeling, and subsequent graft imaging, labeling efficiency was 87\% \pm 6\%. A measured volume of labeled platelet suspension containing approximately 13\% non-platelet-bound isotope was then injected directly into the recipient animals following the preparation of a 100 \(\mu\text{l}\) standard. Additional washing procedures to remove non-platelet-bound isotope were deemed undesirable since they may produce in vitro cell damage. Moreover, in all studies with the scintillation camera, blood pool activities from all sources (platelet and nonplatelet) were a small fraction of total deposited platelet activity and were subtracted using appropriate computer-assisted image analysis routines as described below.

To determine whether the centrifugation procedures resulted in the isolation and labeling of platelets which were representative of the parent platelet population, density separation was performed on platelets harvested from citrated whole blood (10 ml), diluted with a half volume of Ca\(^{2+}\)-free modified Tyrodes-ACD buffer, pH 6.5 containing EDTA (0.5 mM). Following centrifugation at 200 g for 10 minutes, the upper supernatant layer of PRP was removed without disturbing the interface, and the remaining cells diluted to the original volume with Tyrodes-ACD buffer, remixed and centrifuged as before. The second supernatant fraction was harvested and pooled with the initial harvest. This procedure was performed a total of four times; over 94\% of the total platelet population was recovered with minimal leukocyte contamination (<0.01\%).

Percoll (Pharmacia, Uppsala, Sweden) was made iso-osmotic with physiological Tyrodes-ACD solution by adding nine parts (vol/vol) of Percoll to one part of 10x concentrated Tyrodes-ACD buffer, pH 6.5. The osmolarity of the resulting stock solution was adjusted to 295 mOs/kg H\(_2\)O with deionized water. Uniform mixtures of the platelet preparation (4.5 ml) and stock isoosmotic Percoll (5.5 ml) were poured into polycarbonate centrifuge tubes and centrifugation carried out in a 30\° angle-head rotor at 10,000 g for 20 minutes at 22\° C. During centrifugation, platelets moved to a position corresponding to the density of the surrounding medium, i.e., platelets were separated on the gradient formed in situ. Identical tubes containing density marker beads (Pharmacia) were used to calibrate the gradients. Following centrifugation, gradients were fractionated by removing fractions (0.45 ml) from the top of the gradient with an automatic pipette, and the platelet concentration and radioactivity were determined for each fraction. At 1 hour after injection of the labeled platelet preparations, both the labeled and total platelet populations had equivalent density distributions, as illustrated in Figure 2. Thus, the density distribution of labeled platelet activity was representative of the parent platelet population.

Circulating platelet \(^{111}\text{In}\)-activity was determined from 4 ml blood samples drawn before and after graft placement, and collected in 2 mg/ml (ethylenedinitrilo)-tetraacetic acid (EDTA). From each sample, 1.0 ml was used for whole blood \(^{111}\text{In}\)-activity and cell-free plasma determinations, and 1.0 ml was counted for whole blood \(^{111}\text{In}\)-activity. The remaining 2 ml were centrifuged at 3000 g for 30 minutes and 1.0 ml of the supernatant (PPP) was counted for plasma \(^{111}\text{In}\)-activity. All blood and plasma samples were counted using a gamma spectrometer (Nuclear Chicago, Chi-
Plasma activity per milliliter of whole blood was calculated by multiplying the activity per milliliter of plasma by the factor: (1-hematocrit). Plasma activity averaged 13% ± 5% (n = 14) of whole blood activity in samples taken 1 hour following injection of the labeled platelet concentrate. Platelet counts were performed on whole blood by using an electronic platelet counter (Clay Adams UF-100, Parsippany, New Jersey).

Mean platelet survival times were calculated by fitting the disappearance curve of platelet radioactivity to gamma functions as described by Murphy et al. The proportion of labeled platelets remaining within the systemic circulation (i.e., recovery) was calculated from the initial platelet activity per milliliter of whole blood, multiplied by the estimated blood volume (65 ml/kg), and divided by the platelet 111In-activity injected.

Platelet survival curves, assessed following 111In-platelet labeling in eight normal animals, displayed a predominantly linear disappearance pattern (Figure 3). Platelet survival times as determined from the computer-fitting procedure averaged 5.59 ± 0.14 days (± 1 se). Platelet recoveries, determined from samples taken at 1 hour were 79.0% ± 2.8%. Recoveries determined by extrapolating the best fit survival curves to time zero averaged 80.5% ± 2.9%. When the recovery of 111In-labeled platelets was calculated from circulating levels of platelet bound isotope measured at 10 minutes, 20 minutes, and 1 hour following injection of the labeled platelet concentrate in seven additional baboons, values were 81.2% ± 3.3%, 79.3% ± 3.4%, and 78.9% ± 4.2%, respectively (Figure 3). Thus, the recovery of the labeled platelets was immediate and equivalent at all early time points, and demonstrated rapid equilibration without transient platelet sequestration. These values for platelet survival and recovery were in agreement with those previously obtained in baboons using a 51Cr platelet label.

Platelet suspensions were analyzed for ATP and ADP using neutralized perchloric acid extracts and high performance liquid chromatography (HPLC). Platelet-rich plasma (PRP) was prepared from citrated whole blood (10 ml) by three differential centrifugation steps at 200 g for 10 minutes at 22°C. These platelet preparations have been shown to be essentially free from contaminating leukocytes and representative of the total platelet population. Total platelet adenine nucleotides were extracted by the addition of 11.5 M HClO4 (100 μl) to the platelet suspension (1 ml). Cell debris and denatured protein were removed by centrifugation at 2000 g for 15 minutes at 4°C and the supernatant was neutralized by titration with 10.0 M KOH. All neutralized extracts were stored at −80°C prior to analysis by HPLC.

Quantitative nucleotide analysis was carried out using a Spectra-Physics SP8000 liquid chromatograph equipped with a Data System (Spectra-Physics, Santa Clar, California) and coupled to a Gilson variable wavelength UV detector operating at a wavelength of 254 nm. A Partisil 10SAX microparticulate anion-exchange column was used (Whatman, Incorporated, Clifton, New Jersey) and optimal resolution of adenine nucleotides was achieved using the operating conditions previously described.

Blood for platelet factor 4 (PF4) and β-thromboglobulin (βTG) was drawn as 5 ml samples from the arteriovenous shunt into precooled syringes containing 1 ml of ACD, acetylsalicylic acid and prostaglandin E1, 30 mM and 1 μM final concentrations, respectively. Blood was collected before and after placement of each graft. Samples were centrifuged at 45,000 g for 20 min at 4°C within 30 minutes of collection. Then 1.0 ml of the platelet-free plasma was removed and stored at −20°C. Assays for PF4 and βTG were performed by competitive radiomimunoassay. βTG determinations were carried out using a commercially available radiomimunoassay (Amersham, Arlington Heights, Illinois). PF4 was measured by the procedure previously reported by us. To determine the platelet content of PF4 and βTG, the platelets in PRP were lysed with Triton X-100 (1% final concentration). Cell debris was removed by centrifugation at 45,000 g for 20 minutes at 4°C. Samples were then assayed in the same manner as the platelet-free plasma samples.

**Analytical Methods**

Scintillation camera imaging of both gamma photon peaks of 111In (172 keV and 247 keV) has generally required high energy collimation to prevent image blurring, despite a decrease in both sensitivity and spatial resolution. Since platelet-specific activity was not a limiting factor in the present studies, a high sensitivity 99mTc collimator could be used with good resolution by imaging only the lower energy peak of 111In (172 keV peak with a 5% energy window).
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ages of the Dacron grafts, including proximal and distal Silastic segments, were acquired with a Picker DC 4/11 Dyna scintillation camera (Picker Corp, Northford, Connecticut) and stored on and analyzed by a Medical Data System SIMUL computer (Medtronic, Ann Arbor, Michigan) interfaced with the camera. This system permitted simultaneous acquisition and analysis of data in 64 x 64 word mode. Immediately before imaging the graft segments ex vivo, 2- minute images were acquired of the 200 μl sample of platelet concentrate (injection standard) and of a segment of 4.0 mm i.d. Silastic tubing filled with autologous blood and having the same luminal volume as the graft segment (blood standard). All standards and tubings were placed into a groove precisely machined into plexiglass to maintain a linear geometry that was positioned approximately 1 cm from the face of the collimator. The activities of the standards and 10 cm graft segments were counted in the same 3.1 cm x 12.5 cm region of interest (10 x 40 pixels) as defined by image analysis software routines. From the time of graft placement, images were acquired continuously with data storage at 2-minute intervals. Deposited 111In-platelet activity was calculated by subtracting the blood standard activity from all dynamic study images.

In several studies, grafts were placed and imaged sequentially for several days following injection of a single preparation of 111In-labeled platelets. Since circulating 111In-platelet activity was lost continuously through normal physiologic mechanisms, and acutely by serial graft placement, measurements of platelet accumulation were expressed as a graft/blood ratio, defined as the ratio of deposited graft activity divided by the whole blood (circulating) platelet activity within the graft lumen measured at the beginning of each experiment. This measurement was chosen since it is independent of the size of the animal, the amount of isotope injected, or the extent to which the isotope may have decayed. The graft/blood ratio will, however, depend upon the timing or sequence of observations if, between periods of graft placement, platelet functional alterations have occurred as a result of aging in the circulation or prior exposure to thrombogenic surfaces.

To determine the graft/blood ratio, the activity of blood within the graft lumen (1.26 ml) was determined by two separate methods. First, it was calculated directly after imaging the blood standard (1.57 ml blood volume). In the second approach, the activity per milliliter of blood present at the beginning of each experiment was calculated by imaging the injection standard before each experiment, multiplying this value by the CPM per ml of whole blood drawn at the time of the experiment (as determined using a gamma counter at some later time t1), and dividing by injection standard activity (also measured in the gamma counter at t1). All blood samples and standards were counted simultaneously at the end of each series of experiments. In all calculations, radioactivity values refer to platelet activity only, with total blood and standard values having been corrected for the fraction of nonplatelet isotope. In the 36 studies involving graft placement, blood activities as determined from the two methods were equivalent ±8% (± 1% SD, p > 0.5) demonstrating that either method is appropriate for calculating the graft/blood ratio. Subsequent data are presented according to the second approach since the higher activity of the injection standards (vs blood standards) gave more acceptable counting statistics.

Total platelet deposition (labeled plus unlabeled cells) was estimated by multiplying the graft/blood ratio by the factor: graft blood volume (1.26 ml) x platelet concentration per milliliter of whole blood. This computation involved the assumption that the labeled and unlabeled platelet populations were equivalent with respect to graft deposition at all times.

Statistical comparisons were made by using Student's t-test (two-tailed) for paired and unpaired data. All statistical analysis and curve fitting was done using the PROPHET system of the Division of Research Resources, National Institutes of Health. Unless otherwise stated in this report, variance about the mean is given as ± 1 SE.

Results

Effects of Graft Placement on Platelet Viability

Since platelets may undergo biochemical and functional alterations as a result of aging in the circulation, we first evaluated the importance of the delay period between platelet labeling and infusion, and subsequent graft imaging. In six baboons, 111In-platelet deposition was assessed on grafts placed 1, 24, 48, and 72 hours after injection of the labeled cells. All grafts were imaged for 1 hour, and then removed.

Measurements of graft 111In-platelet deposition are shown in Figure 4. Platelet deposition curves were generally sigmoidal, and reached a plateau by 60 minutes. At 1 hour, graft radioactivity was typically 40- to 50-fold greater than the radioactivity circulating within the graft lumen. At all time points, the deposited activity on grafts placed 1, 2, or 3 sequential days after the injection of labeled platelets was equivalent to that observed on grafts studied 1 hour after infusion of the normal labeled platelet population (p > 0.2 in all cases), despite platelet aging in the circulation or the prior placement of one, two, or three grafts.

The disappearance of circulating 111In-platelet activity following graft placement in five animals is shown in Figure 5. Although a reduction in circulating platelet radioactivity was consistently observed following the placement of the graft, the remaining platelets appeared to survive normally. The survival curves that would have resulted without the insertion of vascular graft segments were estimated by correcting the measurements of radioactivity taken on Days 2, 3, and 4 for the acute loss of radioactivity.
resulting from each graft placed previously (Figure 5). All points on the resulting survival curve were within the limits obtained in normal animals.

Reductions in circulating platelet concentration and circulating $^{111}$In-platelet activity were determined for the period the graft was in place (Table 1). Circulating platelet number and platelet $^{111}$In activity decreased approximately 15% following the placement of each graft, i.e., the reduction values were equivalent ($p > 0.5$), demonstrating that the labeled and unlabeled platelet populations were not measurably different with respect to thrombotic platelet utilization in this model.

In five control studies, a $20 \times 3.125$ cm region of interest containing the 10 cm graft segment was imaged, and was subsequently divided into 16 sequential regions with dimensions $1.250 \times 3.125$ cm. The activity in each region was calculated as a fraction of total image activity. Although $^{111}$In-platelet activity appeared higher in distal graft segments, the relative activities in proximal and distal graft segments did not differ significantly (44.7% ± 7.0% and 55.3% ± 7.0% respectively; $p > 0.10$). In general, deposited platelet activity appeared to be uniformly distributed within the graft segment without evidence of localized deposition or thrombus propagation. Morphologic evaluations of grafts exposed to flowing blood for 1 hour demonstrated thrombi rich in platelets with red cells trapped in a fibrin mesh (Figure 6).

**Graft-Induced Release of Platelet Granule Constituents**

In 14 control studies, measurements of plasma levels of PF4 and BTG were performed on blood samples taken before and after graft placement. Baseline plasma levels of each platelet specific protein showed little variation ($p > 0.3$ in all cases), and the values are shown in Table 1. Following graft placement, PF4 and BTG values increased approximately tenfold over baseline values ($p < 0.001$). However, the total platelet content ($\mu$g/10$^8$ platelets) of these proteins as determined from lysed platelet preparations remained unchanged in each case ($p > 0.5$). In addition, the content of ADP and ATP in circulating platelets was not measurably depleted by graft placement ($p > 0.5$, Table 1).

**Discussion**

The present study was designed to assess directly, in a nonhuman primate model, platelet deposition and acute platelet alterations after exposure to Dacron grafts under arterial flow conditions. Dacron vascular grafts were chosen as the thrombogenic surface since these materials have direct application in humans, and since platelet thrombus formation could be initiated under well-defined conditions of flow and geometry. Thus, in the present studies the graft length (10 cm) and period of exposure (1 hour) were selected to produce measurable platelet accumulation without causing a marked and possibly con-

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**Figure 4.** Platelet deposition on grafts placed sequentially. Identical grafts were placed for 1 hour daily in the following sequence: Day 1, (o); Day 2, (•); Day 3, (A); Day 4, (A). No significant daily variations ($p > 0.2$) were observed over 4 days when results were expressed as the graft/blood ratio of $^{111}$In-platelet activity (A) or as total deposited platelets (B). Values are means ±1 se in six animals (Days 1, 2, 3) or four animals (Day 4).

**Figure 5.** Acute reduction in circulating $^{111}$In-platelet activity after graft placement. When the fraction of $^{111}$In-platelet activity remaining after graft placement was corrected for the acute reductions, a normal disappearance pattern was observed (symbols in shaded area). Each point represents the mean of at least four determinations ±1 se.
founding reduction in the circulating platelet count (Table 1).

Since these in vivo studies were performed using platelets labeled with $^{111}$In-oxine in vitro, it was first necessary to demonstrate that the labeled platelets were functionally normal and representative of the parent population. Thus we observed that the recovery of labeled platelets was normal within 10 minutes after infusion into the circulation (Figure 3). Platelet survival curves in normal animals were predominantly linear (Figure 3) and equivalent to results obtained previously using a $^{51}$Cr-platelet label.\cite{2,10} One hour after infusion of the labeled platelet suspension, the labeled and total platelet populations had identical density distributions as determined with Percoll density gradients (Figure 2). These data suggest that the

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**Table 1. Effect of Dacron Graft on Platelets**

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Figure 6. Scanning electron micrograph of thrombus on graft surfaces. After 1 hour, extensive platelet deposition and fibrin strand formation with trapped erythrocytes was evident in control grafts. Bar = 10 µm. 
labeled platelet population was not enriched in either more dense or less dense platelets as a result of platelet harvesting and labeling in vitro. Also, 1 hour after infusion, the labeled platelets were functionally normal with respect to thrombus formation as shown by equivalent reductions in circulating platelet radioactivity and circulating platelet numbers following the insertion of Dacron grafts. Since the labeled and unlabeled platelet populations were equivalent by all tested criteria, total platelet deposition could be calculated from measurements of graft radioactivity. In addition, since these measurements were independent of the timing of graft placement with respect to platelet labeling, this model appears to be an efficient one, (i.e., following a single labeling procedure, grafts may be imaged at daily intervals with equivalent results).

Graft placement, which resulted in the destruction of approximately 15% of the 111In-labeled platelet population, also did not alter the survival, α-granule contents, or dense granule contents of those platelets that continued to circulate. The findings of elevated plasma levels of PF4 and βTG (Table 1) thus imply that α-granule release had occurred only from platelets which had reacted irreversibly with the graft. Since about 75% of platelets removed from the circulation, as determined from platelet counting, were present on the graft after 1 hour (as determined from imaging), the possibility of reversible platelet interactions in addition to graft platelet removal by embolization and lysis cannot be excluded. However, since the viability and function of the circulating platelet pool was not measurably affected, such interactions must be almost totally reversible, or, affect only a small proportion of circulating platelets.

These results are in agreement with previous studies which demonstrated normal platelet ADP/ATP levels in patients and baboons undergoing cardiopulmonary bypass,14,15 but are not in accord with the reported reduction in platelet dense granule contents observed in patients with valvular heart disease and Dacron vascular protheses, and in dogs with chronic aortic grafts.16-18 Since our data are consistent with the hypothesis that acute thrombosis in vivo rapidly produces irreversible platelet removal, we speculate that platelet alterations associated with chronic disorders involving elevated platelet turnover may largely reflect the presence of an increased proportion of younger cells rather than an abnormality acquired during circulation. Under these conditions the functional capacity of platelets has been shown to be diminished in rabbits19 and dogs20 and unchanged in baboons.7,10 The clinical relevance of these observations remains unknown.

In previous studies of 111In-platelet deposition onto vascular grafts in both experimental animals21-26 and humans27-30 the effects of several variables have been studied, including graft type,22,23,28,30 blood-flow rate,25 and the effects of antithrombotic therapy.26,27,28,30 We believe that this model of acute thrombosis is suitable for assessing the effects of other variables and therapies, and for defining systemic blood alterations secondary to platelet thrombus formation on prosthetic surfaces in vivo.

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References

Index Terms: platelets • vascular grafts • platelet release • indium labeling
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