Late, Heparin-Induced Bleeding after Retrograde Arterial Catheterization

By J. David Bristow, M.D., Arthur J. Seaman, M.D., Frank E. Kloster, M.D., Rodney H. Herr, M.D., and Herbert E. Griswold, M.D.

SUMMARY
Three patients who had valve prostheses were given heparin after percutaneous retrograde aortic catheterization from the femoral artery. The drug was given prophylactically in one case and because of the development of signs of systemic embolism soon after catheterization in the other two. After 3 or more days of heparin therapy, serious bleeding developed at the site of percutaneous catheter entry. The timing and incidence of this complication are in marked contrast to experience with this procedure in individuals who did not receive heparin.

Preliminary experience is presented from right and left heart catheterizations in patients whose prothrombin-proconvertin times were allowed to remain in or near the therapeutic range. No hemorrhagic complications were observed.

Additional Indexing Words:
Hemorrhage Anticoagulation Phenindione Warfarin

Patients who receive long-term anticoagulant therapy and require cardiac catheterization present a difficult problem. Until 1967 it was our practice to discontinue administration of dicumarol-type drugs for a few days before the procedure to allow clotting functions to return toward normal. In some individuals with predisposition to thromboembolism, heparin was then given during the first 3 or 4 days after catheterization, while the prothrombin time was readjusted to the desired range.

It is our purpose herein to describe late, potentially disastrous hemorrhage from such heparin therapy after percutaneous retrograde aortic catheterization from the femoral artery. In addition, we wish to report preliminary experience with right and left heart catheterization in patients with prothrombin times in the therapeutic range, obviating the need for complete interruption of anticoagulant therapy or the possible need for heparin afterward.

Report of Cases

Case 1
A 39-year-old woman had mitral replacement with a Starr-Edwards prosthesis 18 months before cardiac catheterization. She received phenindione until a few days beforehand; the day before the procedure the prothrombin-proconvertin (PP) time had risen to 74%.1 Transseptal left atrial catheterization, brachial arterial cannulation, and percutaneous transfemoral retrograde arterial catheterization with a 6 F Teflon Gensini catheter were performed.2–4 Four hours after completion of the procedure she became lethargic and left hemiparesis had developed; 4 hours later she was nearly free of neurological abnormality. It was presumed that she had sustained an embolus from her prosthesis to a branch of the middle cerebral system. During the period of her overt neurological findings, administration of heparin was begun with a dose of 75 mg given intravenously and 75 mg

From the Divisions of Cardiology and Hematology, Department of Medicine, University of Oregon Medical School, Portland, Oregon.

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was given intramuscularly every 6 hours. Treatment with phenindione was resumed the next day. The dose of heparin was changed to 100 mg subcutaneously on the second postcatheterization day. On the fourth day a large right femoral hematoma developed at the site of insertion of the arterial catheter. At this time the Lee and White coagulation time was over 40 minutes and the PP time was 29%. A compression dressing was applied and treatment with heparin was discontinued. Phenindione was continued. The hematocrit was 37% before the hematoma and 24% when bleeding ceased that day. The patient recovered completely without transfusion or operation.

Case 2
A 61-year-old man was admitted 25 months after aortic valve replacement for evaluation of a leak around the prosthesis. Use of anticoagulants had been stopped ahead of time and on the day before the procedure the PP time was 80%. Brachial arterial cannulation, transseptal left heart catheterization, and retrograde left heart catheterization from the femoral artery were performed without event. At the end of the procedure, however, the patient developed aphasia and right hemiparesis. Heparin was administered on the first postcatheterization day, 100 mg every 6 hours subcutaneously, and 30 mg of warfarin was given also. The dose of heparin was increased to 115 mg every 6 hours on the second day because of relatively normal Lee and White coagulation times. On the third day after the procedure a large right femoral hematoma became apparent. The hematocrit fell from 38 to 22% despite transfusion of 1,000 ml of blood; 1,500 ml more blood was required to maintain a stable state. The PP time was 5%. Administration of heparin was stopped, protamine was given, and compression dressings were applied. The bleeding then stopped. The patient died of the cerebral problem 10 days after the catheterization. Autopsy demonstrated left cerebral infarction due to cerebral arterial thrombosis.

Case 3
A 51-year-old woman had mitral and tricuspid replacement with prostheses 8 months before the admission under consideration. Systemic arterial hypertension had become progressively severe postoperatively; a typical blood pressure was 190/114 mm Hg. She received warfarin therapy chronically.

On the day before renal arteriography the PP time was 48% and no warfarin had been given that day or on the day of the test itself. A percutaneous transfemoral retrograde catheterization of the aorta and renal arteries was performed without incident and arteriograms were obtained. On that evening heparin was given (150 mg subcutaneously every 8 hours). In addition 30 mg of warfarin was administered. On the third postcatheterization day a right femoral hematoma developed. At that time the Lee and White coagulation time was longer than 30 minutes and the PP time was between 17 and 30% (values for days 2 and 4). The hematocrit fell from 34 to 18% on the following day and the patient was given 750 ml of packed red cells. When the hematoma developed, she received 5 mg of vitamin K₁ oxide and 25 mg of protamine intravenously. Bleeding stopped, but a long complicated course eventuated in surgical drainage of the inguinal area 5 weeks later. She then recovered completely.

Discussion
We are aware of only four patients in our hospital who have received heparin soon after diagnostic catheterization. As described, three of these had serious bleeding at the femoral arterial site of percutaneous catheter entry, beginning on the third or fourth day after the procedure. The fourth patient received heparin for only 1 hour during cardiopulmonary bypass for excision of a left atrial myxoma and had no bleeding from the entry site for retrograde catheterization performed earlier that day. All three patients who received heparin for 3 or more days bled in a quantity sufficient to decrease the hematocrit 13 to 16 points. This remarkable incidence contrasts both in frequency and timing with postcatheterization bleeding observed in other patients. In the past 36 months there have been 314 percutaneous retrograde left heart catheterizations from the femoral artery in our laboratory in patients who did not receive heparin. One hematoma which required treatment developed and became evident within a few hours after the catheter was removed. Others have observed more immediate bleeding. The lateness of the hemorrhages we observed suggests lysis by heparin of the small clot which plugged the femoral arterial puncture site.

We recognize that heparin was not the only anticoagulant administered to the three patients described. All had been given priming or maintenance doses of prothrombin depressing drugs as well and the PP time was...
HEPARIN-INDUCED BLEEDING

undesirably low at the time of hemorrhage in one patient. Nonetheless, we believe that heparin is responsible for their bleeding on several counts. Many other patients have had comparable ranges of PP times during the first 4 days after similar catheterizations without hemorrhage. Furthermore, treatment with hypoprothrombinemic drugs was continued in our three patients despite the hemorrhage. Bleeding stopped when heparin therapy was discontinued, with or without administration of protamine. Finally, an increased incidence of bleeding has followed the use of heparin in other situations. For example, heparin alone or heparin initiation of warfarin therapy led to a significant increase in the frequency of bleeding as contrasted with warfarin alone in controlled studies in patients with acute myocardial infarction.8, 9

The problems we have described were related in one or another way to the fact that anticoagulant therapy had been discontinued to permit cardiac catheterization. In view of these difficulties, we have explored the possibility of performing these procedures without raising the PP time to normal. During the past year anticoagulant drugs have been omitted for 1 day beforehand, no vitamin K has been given, and catheterization has been done regardless of the PP level. Ten patients have been managed in this way and their procedures have included right heart entry in all, percutaneous retrograde arterial left heart in nine, transseptal left heart in four, and direct left ventricular puncture in two.10

The PP times on the day of their studies ranged from 4 to 48%, with values below 22% in six. No difficulties with bleeding developed.

Although this experience is not extensive, it does demonstrate that, despite low PP times, these manipulations are possible without hemorrhage and we believe that further exploration of the method is justified. Anticoagulants are withheld for 1 day to assure a rising prothrombin concentration should a complication ensue, yet allowing prompt readjustment to the desired level after catheterization. A prolonged period without anticoagulant protection thus can be prevented in patients who have significant risk of thromboembolism, and the possible need for heparin therapy (with its substantial hazard) can be avoided as well. This approach is encouraged by published descriptions of major surgery during hypoprothrombinemic anticoagulation without significant increase in bleeding.11-16 We believe that further experience may allow the routine recommendation of this regimen for anticoagulated patients who require cardiac catheterization.

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References


Hypotheses

Crux of Arguments

The formulation of a hypothesis carries with it an obligation to test it as rigorously as we can command skills to do so. There was no sign of any such sense of obligation in Burnet’s Sacred Theory: to explain the phenomena it was designed to explain was judged evidence enough. It satisfied curiosity in much the same way as a mother’s desperately ad hoc answers satisfy the insistent questioning of a child. The child is not interested in the content of the answer: he asks as if he were under an instinctual compulsion to do so, and the act of answering completes a sort of ritual of exploration. But when curiosity is satisfied it is discharged: formulation of a hypothesis may act as a deterrent rather than as a stimulus to inquiry—a danger the earlier critics of the use of hypotheses were fully aware of.—P. B. Medawar: The Art of the Soluble. London, Methuen & Co. Ltd., 1967, p. 145; also distributed by Barnes & Noble, Inc., New York.
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