Pulmonary Bed Sequestration of Neutrophils During Hemodialysis

By Michael Toren, John A. Goffinet and Leonard S. Kaplow

A severe, transient granulocytopenia occurs shortly after the beginning of hemodialysis in the dog, as has been previously shown in man. Simultaneous blood sampling across the pulmonary vascular bed indicates that the process of granulocyte removal begins almost instantaneously and that the pulmonary vascular bed is a major site of granulocyte sequestration.

A dramatic transient and rapidly reversible neutropenia occurs during the first few minutes in patients undergoing hemodialysis. This neutropenia is followed by an increase in the number of band neutrophils and a return to near normal circulating leukocyte levels approximately 1 hour after the start of dialysis. The phenomenon is not associated with chills, fever or other symptoms. In our original report, we showed that the disappearance of granulocytes was not the result of their destruction during passage through the dialyzer and could not be attributed to heparin or to the pump mechanism. We postulated that a humoral factor formed in the dialyzer produced a profound decrease in circulating granulocytes virtually immediately on being infused into the patient and that the granulocytopenia was probably due to sequestration of cells in the lungs. The present report shows that dialysis-induced neutropenia may be experimentally elicited in healthy dogs and that under such conditions, sequestration of large numbers of neutrophils does indeed occur in the lungs.

Materials and Methods

Healthy adult, dewormed and quarantined mongrel dogs (10–25 Kg.) were anesthetized with sodium pentothal (30 mg./Kg. I.V.). Anti-coagulation was maintained by sodium heparin, 200 units/Kg. I.V. initially and 100 units/Kg. I.V. thereafter.

Under aseptic conditions, the femoral artery and vein were cannulated with polyvinyl catheters. A right thoracotomy was performed and a sterile No. 10 Bardic plastic catheter

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Fig. 1.—Dialysis-induced leukopenia in dogs. Changes in peripheral blood total and neutrophilic leukocyte counts in three dogs undergoing hemodialysis. The bars labeled A represent control counts prior to dialysis. The bars labeled B represent maximum recorded leukopenia and occurred 4,3 and 3 minutes after the start of dialysis for dogs 1,2 and 3, respectively.

was placed in the pulmonary artery by way of the azygous vein, the right atrium and the right ventricle. The position of the catheter was ascertained by palpation and confirmed by autopsy.

A Travenol Ultra-Flow 145 dialyzer was used in conjunction with a Sams roller pump at a circulation rate of 100 ml./min. The dialyzer and tubing were primed with saline and the dialysate was prepared from a commercially available 35 : 1 concentrate (McGaw Hemotrate-K, formula 3).

Changes in total leukocyte counts across the pulmonary vascular bed were expressed as per cent change derived by the formula:

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\frac{\text{femoral artery W.B.C.} - \text{pulmonary artery W.B.C.}}{\text{pulmonary artery W.B.C.}} \times 100.
\]

Six femoral artery to femoral vein hemodialyses were performed on four dogs. Systemic arterial blood during dialyses was collected from a rubber cuff sampling device on the arterial tubing. However, control samples, prior to dialysis, were drawn from a sterile, siliconized three-way stopcock attached to the femoral artery cannula. Simultaneous blood samples from the pulmonary artery and femoral artery were taken at 1,2,3,4,5,7, and 10 minutes during four 15 minute dialysis periods in two dogs and at shorter intervals in two additional dogs dialyzed for 30 minute periods. Femoral artery blood was considered equivalent to pulmonary vein blood and differences in leukocyte counts between the pulmonary and femoral arteries were considered to be entirely due to changes across the pulmonary vascular bed, i.e., there was considered to be no change in cellular composition during passage through the heart chambers and aorta.

Total leukocyte counts were performed on a Coulter Model A automatic cell counter.
Fig. 2.—Pulmonary bed sequestration of leukocytes. Per cent changes in total leukocyte counts across the pulmonary vascular bed (see text for formula for derivation of per cent changes). The range and mean of per cent changes during 10–30 minute control predialysis periods is represented by the open bar (labeled C). The solid bars denote the per cent change across the pulmonary bed during each of the first 5 minutes after the start of dialysis.

Differential white blood cell counts were performed on slide preparations stained with Wright’s stain.

Results

During all six dialysis periods there was a rapid and profound leukopenia beginning 1 minute or less after the start of dialysis, similar to that previously reported in humans. Within the first 5 minutes of dialysis, total circulating granulocyte counts, obtained from both the femoral artery and the pulmonary artery, dropped to less than 20 per cent of the predialysis levels (Fig. 1).

Prior to the start of dialysis, no significant differences in leukocyte counts were observed between the pulmonary and femoral blood samples. The mean change during 29 predialysis control periods was 0.17 per cent, with a range of + 16 to − 12 per cent. The median change was + 1.0 per cent. With the onset of dialysis, a marked and highly significant difference in leukocyte counts across the pulmonary vascular bed was observed. The maximal difference occurred 1–4 minutes after the start of dialysis and averaged − 54.5 per cent, with a range of − 48 to − 67 per cent (Fig. 2). Analysis of differential cell counts indicated that these changes were due almost exclusively to a decrease in the number of granulocytes.

Discussion

The present studies show that hemodialysis-induced leukopenia occurs in dogs, as well as in man. The rapidity and the profundity of the fall, primarily due to removal of cells of the granulocytic series, are comparable in dog and in man, strongly suggesting that similar pathogenetic mechanisms apply. The dog may therefore serve as a suitable experimental model for study of this phenomenon.

The changes in systemic and pulmonary arterial leukocyte counts during dialysis can only be accounted for by sequestration of neutrophils by the
pulmonary vascular bed during the first few minutes of dialysis. When compared to changes in W.B.C. during the control period, the percentage change observed during dialysis is significant at the 0.001 level. The magnitude and rapidity of the per cent change across the pulmonary bed suggest strongly that the lungs play a major role in effecting the leukopenia. However, one cannot conclude from the data that sequestration of neutrophils occurs in the lungs only.

Because of the experimental design, changes across the pulmonary vascular bed may have actually been underestimated. Transit times from the pulmonary artery to femoral artery were neglected. In order to analyze the same sample as that obtained at the pulmonary artery, it would have been necessary to draw blood from the femoral artery 10–15 seconds after sampling from the pulmonary artery. During the first few minutes of hemodialysis, when the white blood count was falling rapidly, this would have yielded even lower values for the femoral artery samples, resulting in a more dramatic change across the lungs. We elected to avoid this potentially complicating factor, however, because of the difficulty in precise timing and to avoid possible false positive biasing of results.

The leukopenia induced by dialysis due to pulmonary sequestration of neutrophils is more intense and occurs more rapidly, but is otherwise very similar to the leukopenia evoked by pyrogenic materials and by colloidal suspensions. Weisberger, et al., using 32P-labeled leukocytes demonstrated marked radioactivity in the pulmonary bed following intravenous injection of 32P-labeled peritoneal exudate leukocytes into rabbits. Unlike pyrogenic reactions, dialysis-induced leukopenia is not associated with fever and chills. The present study confirms previous concepts of the role of the lungs as a sequestering site for leukocytes.

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REFERENCES

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