OBSERVATIONS ON VENOUS ENDOTHELIAL INJURY FOLLOWING THE INJECTION OF VARIOUS RADIOGRAPHIC CONTRAST MEDIA IN THE RAT*

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It has long been recognized that contrast media injected into the blood stream may produce serious damage in the tissues served by the injected vessel. Angi spasms and thrombosis have been blamed, but the former is difficult to demonstrate and the latter rarely has been observed clinically or experimentally. Several observers have demonstrated increased permeability of the vascular bed supplied by an artery into which contrast medium had been injected, and they suggested that the fundamental lesion caused by the contrast medium is damage to the wall of the vessel. 1, 2

The purpose of this study was to determine, firstly, whether or not contrast media would damage the endothelium and, secondly, to compare the endothelial toxicity of six different contrast media.

METHOD

Forty-nine Wistar rats of both sexes (180–230 gm.) were used in this experiment. The following contrast media were studied: Neo-Iopax (75 per cent), Urokon (70 per cent), Diodrast (70 per cent), Miokon (70 per cent†), Hypaque-M (90 per cent) and Renografin (76 per cent). Normal saline was used in control animals. After preliminary studies with Urokon (70 per cent), the following technique was developed.

Each animal was anesthetized with ether and placed in a supine position. One ml. of the contrast medium to be tested then was injected into the left lateral vein of the tail over an interval of 30 seconds. The rat then was kept in the supine position under ether anesthesia for 5 minutes. At the end of this time, the animal was turned to the prone position and allowed to regain consciousness. Thirty minutes from the time of injection, the animal was anesthetized again with ether and the endothelium of the inferior vena cava and the common iliac veins was stained and fixed in situ by the perfusion technique described previously. 7

RESULTS

Four rats died during or shortly after the injection of the contrast medium because of respiratory failure. There was no evidence of neurological lesions or other toxic effects in any of the surviving animals.

The lesions in all cases were confined to a well defined band of endothelial cells lining the dorsal surface of the left common iliac vein and the inferior vena cava (thoracic and abdominal portions).

The endothelium of the lateral and ventral walls was normal (Fig. 1) as was the endothelium of control rats injected with normal saline.

Neo-Iopax (75 per cent) and Urokon (70 per cent). These two contrast media produced the most severe and extensive lesions. The lesion consisted of a band of almost completely desquamated endothelium (Figs. 2 and 3) running from the entrance of the vein of the tail to the right atrium.

The central zone of the lesion was covered partially by shrunken, partly desquamated endothelial cells lining the dorsal surface of the left common iliac vein and the inferior vena cava (thoracic and abdominal portions).

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The central zone of the lesion was covered partially by shrunken, partly desquamated endothelial cells (Fig. 4). Clumps of platelets were seen attached to the lesion (Fig. 5). Five of the 6 rats injected with Neo-Iopax had white (basophilic) thrombi on their lesions and in 1 of these animals three typical coraline thrombi were present.

Hypaque-M (90 per cent), Miokon (70 per cent), Diodrast (70 per cent) and Renografin

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† Prepared from Miokon (50 per cent) by evaporating to dryness and reconstituting with water.
The lesion produced by these agents consisted of a band of scattered destruction of endothelial cells (Fig. 6) which was most severe in the left common iliac vein and at a point just distal to the liver. In sites of the damaged cells, distorted endothelial nuclei were seen as well as the characteristic silver staining of the underlying layer of smooth muscle (Fig. 7).

Each specimen was graded as to the severity and extent of the lesion (Table 1).

**DISCUSSION**

Our observations on the relative endothelial toxicity of the contrast media studied are in agreement with the studies on neurotoxicity by Tindall et al., Lance and Killen, and also the study on nephrotoxicity by Killen and Lance. This would suggest that the neurotoxicity and nephrotoxicity of these compounds may be caused primarily by their toxic effect on the vascular endothelium.

Hol and Skjerven and Tindall et al. have demonstrated the effect of gravity on the distribution of contrast media in aortography in dogs. The present study demonstrates the layering out of these media. We have injected rats in the prone position and as a result have found the lesion on the ventral surface of the vena cava.

The lesions produced by the apparently