Thromboembolic Sequelae to Indwelling Silastic Cannulas in Sheep Arteries

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Summary

In sheep, chronic arterial cannulation with Silastic has led to thrombus formation and to intimal fibroplasia of a type not previously reported. Concurrent infection resulted in septic embolization to the brains and eyes on the same side as the cannulated vessels. The histopathology is described in detail.

Because they evoke minimal tissue reaction,1 Silastic prostheses have become increasingly popular as chronic implants. Within the lumina of vessels, however, Silastic cannulas often result in thrombotic complications.2,3 At this institution, thromboembolic syndromes developed in six experimental sheep within 2 months after insertion of indwelling arterial Silastic cannulas. Histopathological studies were carried out on these sheep in an effort to define the pathogenesis of the lesions and to confirm their association with the arterial cannulas.

Clinical Findings

Autoclaved Silastic cannulas (Dow-Corning) were surgically implanted in either the right or the left carotid arteries of six healthy, 9-month-old Hampshire sheep of both sexes. The cannulation was done aseptically through a small slit in the artery, which was temporarily occluded. After being attached to the artery with a silk purse-string suture, the cannula was fixed in place with adjacent fascia. The remaining cannula was then threaded subcutaneously to an outlet between the scapulae, where a 2-way stopcock was
attached and anchored to the skin. Cannulas were routinely flushed with heparinized saline each time they were used.

At intervals varying from 10 to 62 days after cannulation, the animals became progressively listless, anorectic, and febrile. Rectal temperatures as high as 107° were often associated with ophthalmic lesions and clinical signs of a disorder in the central nervous system. The eye lesions varied in severity from simple conjunctivitis to fulminating panophthalmitis with descemetocele formation; they occurred consistently on the same side as the cannula. Neurologic signs consisted of ataxia or head pressing.

Clinical laboratory studies done on several animals showed moderate elevation of the serum levels of glutamic oxalacetic transaminase (to 194 Reitman-Frankel units), suggesting nonspecific tissue necrosis. White blood cell counts commonly revealed mild to moderate leukocytosis, the result of an absolute neutrophilia. Blood cultures were negative.

Gross Necropsy Findings

All the animals were killed by injections of sodium pentothal. At necropsy, the gross lesions were found to be restricted to the carotid arteries, the brain, and the eyes.

The chronically cannulated carotid arteries had irregular, firm, nodular thickenings, often exceeding 1 cm in diameter. In some sheep, arterial thrombosis was complete, although in most cases the cannulas had kept the lumens patent. Gross changes observed in the brain included clouding of the meninges, focal areas of hemorrhage, and foci of cortical malacia in the lateral and ectolateral gyri. Cut surfaces showed subcortical abscesses, diffuse hemorrhages, and an overall decrease in the white matter.

Two of the six sheep had unilateral panophthalmitis, the anterior and posterior chambers being filled with purulent exudate; the lens, iris, and cornea were destroyed. In the remaining sheep, the eyes were grossly normal or showed varying degrees of conjunctivitis and keratitis.

Samples of ascitic fluid, right ventricular blood, cerebrospinal fluid, liver, and aspirates from the posterior chambers of two grossly affected eyes were examined bacteriologically. *Bacillus cereus* was isolated from all samples.
Histopathological Findings

Tissues taken at necropsy were fixed in 10% neutral buffered formalin. The eyes were removed immediately after death and were fixed in Helly's solution. All tissues were sectioned at 5 μ and were stained with hematoxylin and eosin. Selected sections were stained with Masson's trichrome, periodic acid-Schiff (PAS), Alcian blue-PAS, Verhoeff's van Gieson, phosphotungstic acid hematoxylin, Brown and Brenn's stain, Mallory's reaction for iron, Luxol fast blue-PAS, and alizarin red-S. Formalin-fixed blocks of frozen tissue were cut at 8–10 μ on a cryostat and stained with Sudan black-B for lipids.

Arteries

Two types of arterial lesions were seen: Mural thrombi and pads of intimal fibroplasia. Thrombogenic lesions, characterized by sessile intimal plaques or polypoid projections into the lumen, were seen as early as 10 days after cannulation. Histopathological examination of such areas showed a marked increase in Alcian-blue intensity with absence of PAS activity; the presence of hemosiderin-

![Image](https://example.com/image.png)

Fig. 1. Small area of subendothelial fibroblastic proliferation, associated with a dense accumulation of hemosiderin-laden macrophages (arrow) and splitting of the internal elastic lamina. Verhoeff's van Gieson stain, × 200.
laden macrophages suggested that hemorrhage had occurred (Fig. 1). Lipid could not be detected. Changes at this prethrombotic stage were restricted to the tunica intima; except for splitting of the internal elastic lamina (Fig. 1), the remainder of the artery was not remarkable.

When mural thrombi were present, they were composed of laminar accumulations of fibrin mixed with platelets and debris (Fig. 2). In severely affected arteries, organizing thrombi were associated with generalized changes in the arterial wall such as subendothelial fibroplasia, edema, angioblastic proliferation, focal areas of hemorrhage, smooth muscle degeneration, fragmentation of elastic fibers, and occasional foci of calcification. Fat-laden macrophages and endothelial cells could be seen in most thrombosed vessels. Although some thrombi contained gram-positive rods, organisms were not found in the wall of the thrombosed arteries. The walls were diffusely infiltrated, however, with a mixed population of lymphoid cells.

Early intimal fibroplasia was characterized as a small, sessile pad

Fig. 2. A typical mural thrombus characterized by laminar deposits of fibrin and platelets. Phosphotungstic acid hematoxylin, \( \times 11 \).
of subendothelial fibroblasts surrounded by an increased amount of material that stained with Alcian blue. These lesions were detected as early as 23 days after cannulation.

More advanced lesions were characterized by exaggerated proliferation of fibroblasts, which focally increased the thickness of the tunica intima until one fourth to one third of the lumen was occluded (Fig. 3). Despite the size of the subendothelial lesion, the endothelium remained fairly intact and thrombus formation was not observed. The fibroplastic area stained intensely with Alcian blue but showed no PAS activity. In some cases, portions of the lesion closest to the internal elastic lamina contained areas of angioblastic proliferation, occasional hemorrhages, and accumulations of iron and calcium. Lipid was never found.

Eyes

In animals with mild ophthalmologic changes, lesions were seen primarily in the choroid and cornea and were characterized by intense congestion, subacute choroiditis, and acute keratitis. In the severely

Fig. 3. Massive intimal fibroplasia. Note that the lesion is restricted to the tunica intima. Verhoeff's van Gieson stain, × 27.
affected eyes, internal structures were almost totally destroyed. Corneas were edematous and contained numerous small vessels and diffuse infiltrates of polymorphonuclear leukocytes. Anterior chambers were filled with proteinaceous debris, polymorphonuclear leukocytes, and degenerating fragments of lens and iris. Filtration angles were invariably blocked and fibrinous adhesions were present throughout the anterior chambers. The retinas were completely destroyed, and the exudate-laden posterior chambers were bounded by indistinct, edematous choroids infiltrated with mixed lymphoid cells. Inflammatory changes in the optic discs and the optic nerves were minimal.

**Brain**

Intracranial lesions were characterized by varying stages of suppurative meningoencephalitis. The meninges over most of the brain were edematous and infiltrated with mononuclear cells; meningeal vessels were congested and occasionally contained emboli (Fig. 4). Vasculitis associated with heavy cuffs and with infiltrates consisting of mixed inflammatory cells were found throughout the cerebrum and cerebellum. Large hemorrhagic areas and foci of encephalomalacia were scattered throughout the brain. Demyelination and prominent accumulations of gitter cells were present in malacic areas.

![Fig. 4. Section of a brain showing numerous cortical abscesses and a degenerating meningeal vessel containing an embolus (arrow). Hematoxylin and eosin, × 60.](image-url)
Several sheep had one or more large subcortical abscesses characterized by accumulations of eosinophilic debris and polymorphonuclear leukocytes; zones of malacia surrounded these accumulations. Gram-positive rods were identified in these lesions.

Discussion

In both animal and human subjects, thrombosis has been one of the major problems associated with the use of Silastic cannulas in arteries and veins. The pathogenesis appears to be related to a small endothelial tear or focal denudation of endothelium during cannulation or manipulation. Such damaged areas soon acquire fibrin tags, which thicken rapidly as a result of successive laminar deposits of fibrin and debris. In chronic cases, organization of a thrombus eventually occurs. The arterial wall underlying a thrombus generally contains degenerating or necrotic intimal or medial elements such as elastic fibers and smooth muscle cells. Increased thickness of arterial walls in other areas is believed to be the result of smooth muscle hypertrophy and focal fibrosis at injured sites.

In our sheep, occasional thrombi were found to contain gram-positive rods believed to have been introduced when the cannulas were flushed. The meningoencephalitis and panophthalmitis which occurred in some of these sheep are believed to be the result of septic embolization from the arteries. This theory is supported by the fact that the lesions in both the eye and the brain consistently occurred ipsilaterally with the cannulated artery. This is the first report of embolic sequelae from Silastic cannulation, although others have reported infections of clots within cannulas.

The intimal fibroplasia found in these sheep has not previously been described in association with Silastic cannulas. Intimal cushions or pads composed primarily of foamy macrophages or hypertrophic smooth muscle cells have been reported in a variety of species, and it has been suggested that these may be sites of predilection for the formation of atheromatous plaques. The characteristics of the intimal pads found in this study are as follows:

1. They were composed almost entirely of fibroblasts associated with increased amounts of ground substance.
2. At no stage of their development did they contain smooth
muscle cells, foamy macrophages, PAS-positive deposits, or lipid.

3. The fibroplasia occurred exclusively within the boundaries of the internal elastic lamina.

These characteristics suggest that the pathogenesis of this intimal fibroplasia is completely different from that of other types of arterial plaques. The occasional angioblastic activity and accumulations of iron and calcium at the level of the internal elastic lamina of these fibroplastic pads suggest a traumatic etiology, although the role of infection cannot be ruled out.

The findings of this study suggest the need for greater caution when the use of Silastic cannulas in larger domestic animals is being contemplated. The frequent development of mural thrombi in vessels cannulated with Silastic, coupled with the opportunity for the accidental introduction of bacteria, provides a potentially lethal combination.

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References


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