Experimental Carotid Ligation Followed by Aneurysmal Formation and Other Morphological Changes in the Circle of Willis

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The circle of Willis is of considerable importance in ensuring a continuous blood supply to the brain. In a young person with a well-developed circle of Willis, no serious effects follow the occlusion of one of the carotid or vertebral arteries, but in old people a thrombotic or embolic occlusion of a carotid artery is a very common cause of cerebrovascular incidence.\(^4,5,11,15\) The shape of the circle of Willis in the newborn is different from that in the adult. Thus the posterior communicating arteries, and also those portions of the anterior cerebral arteries belonging to the circle of Willis, are relatively narrower in the latter,\(^4,14\) and this may be a contributory factor in the development of intracerebral vascular lesions.\(^10\)

**Material and Methods**

Forty-two rabbits were used. Of these, 22 were 3 weeks old and came from 7 litters, while the remaining 20 were about 1 year old (weighing 2,500–3,000 gm.).

Ten young rabbits and 10 old ones were chosen at random. In these animals the carotid artery on one side of the neck was ligated. In the rabbit, the internal carotid artery is very small and branches from the common carotid artery close to the skull. For practical reasons, a ligature was applied to the common carotid before the internal carotid artery was dissected free and ligated. Thus on one side of the neck both the common carotid and the internal carotid arteries were ligated.

In 2 young rabbits, the carotid artery on both sides of the neck was ligated.

In the remaining rabbits, a dummy operation was performed as a control. This operation consisted in free preparation of one common carotid artery, which then was replaced and the incision was sewn up again.

Half of the rabbits were sacrificed 1 month after operation, and the other half 5 months after operation. A total of 2 rabbits died earlier.

After the animals had been sacrificed, the site of operation was inspected to check whether the ligation had been successful. In one half of the cases, the brains, with all large intracranial arteries intact, were placed in Bouin’s fixative. In the other half, the alternative procedure of injecting the fixative under a slight pressure (30 mm. Hg) into the aorta was adopted, so that the cerebral arteries were fixed in a distended state to eliminate the folding and contraction post mortem. After fixation, the arteries in all cases were removed from the brains and divided into short segments, each comprising only one point of branching. Detailed sketches of the segments were made in order to facilitate the reconstruction of the serial sections. The segments were stained with cosin to assist the embedding and serial-sectioning procedures. The sections were stained with various stains for elastin in combination with van Gieson or azan.

**Results**

The regular location and the normal histological appearance of defects of the media and of physiological cushions of the intima in the circle of Willis of the rabbit (Fig. 1A) already have been investigated.\(^7\) The sizes of cushions and defects show certain variations between individual rabbits, and in about one third of the animals, some cushions or defects are absent. The calibres of the arteries of the circle of Willis show much smaller individual variations in rabbit than in man.

Following the carotid ligation exceptionally large defects of the media were found, especially at the anterior end of the basilar artery but also at the distal end of the junction between the internal carotid and the posterior communicating arteries on both sides. The defects in the rabbits with a carotid ligature were considerably larger than those in the rabbits not ligated.

Six of the large defects found in the ligated rabbits showed a considerable bulging of the
arterial wall and a defective internal elastic lamina, as in a saccular aneurysm (Fig. 2). All these bulging defects were located on the basilar and posterior cerebral arteries. Both rabbits that had been treated with bilateral carotid ligation showed a strongly bulging defect of the media at the anterior end of the basilar artery. Two of the aneurysmal defects had been fixed by the injecting method.

Following carotid ligation, changes in the location and in the size of the cushions of the intima also were observed. At the junction of the two anterior cerebral arteries (rabbits usually have only one anterior cerebral artery distal to the circle of Willis) cushions were found in 12 of the 20 rabbits carrying unilateral ligation, and in 11 of the 18 controls. All the cushions in the ligated animals were situated mainly in the proximal region of the anterior cerebral artery on the ligated side (Fig. 1B). The cushions in the controls were situated as in Fig. 1A, with the exception of one small one located distal to the junction. In all cases extremely voluminous cushions were found on the ligated side at the junction between the internal carotid and the posterior communicating arteries. At the corresponding junction on the opposite side, extremely small cushions were found in 8 cases, while in the remaining 12 no cushion was detected. The volumes of the cushions were determined by inspection of the serial sections, and a significant difference (p = 0.04) occurred between those on the ligated side and those on the side not ligated. The cushions at the anterior end of the basilar artery also showed marked changes after ligation of the carotid. On the ligated side, no, or only extremely small, cushions were found. The cushion on the side of the basilar artery opposite to the ligation was large in all cases. In addition, a new cushion often was found at the posterior end of the posterior communicating artery on the side not ligated. The histological character of the cushions was mixed muscular-elastic, although the proportions of smooth muscle to elastic tissue varied somewhat (Fig. 3).

In all the ligated animals, the calibre of the posterior communicating artery was greater on the side carrying the ligature. The cross-sectioned area (estimated by inspection of the histological sections) was significantly greater (p = 0.02) on the side ligated than on that not ligated. The difference was more accentuated in the rabbits sacrificed after 5 months than in those sacrificed after 1 month.

Although the common carotid artery had been ligated at the neck, several well-developed anastomoses were found between the internal and external carotid systems on the side bearing the ligated artery. The direction of blood flow in these anastomoses was not investigated. The largest anastomosing channels between the external and the internal carotid systems of the ligated side were the ophthalmic, the anterior meningeal and the middle meningeal arteries. The ophthalmic artery on the ligated side showed an increase in calibre which was almost of the same magnitude as that of the posterior cerebral artery (cf. above).

Microscopic preparations of the wall of the arteries that exhibited an increase in calibre (the posterior communicating, ophthalmic

Fig. 1. (A) Normal circle of Willis in rabbit. The physiological intimal cushions and medial defects are indicated by the letters c and d respectively. (B) The circle of Willis 5 months after ligation of the left internal carotid artery. The posterior communicating and the ophthalmic arteries of the ligated side, and the internal carotid artery of the opposite side, show an increase in calibre. Defects and cushions are found at locations differing from those in Fig. 1 (A). The defects in general are larger. Some defects situated at the anterior end of the basilar artery show aneurysmal bulging.
Effects of Carotid Ligation on Circle of Willis

Fig. 2. Defects in media (arrows). In parts of these the arterial wall bulges as in an aneurysm. Aldehyde-fuchsin and van Gieson stains. (A) $\times$190; (B) $\times$290; (C) $\times$360.

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and meningeal arteries of the ligated side revealed a thickening of the wall caused by muscular hypertrophy of the media (Fig. 4).

In the rabbits ligated at an early age, the cerebral hemisphere seemed to be smaller on the ligated side than on the opposite side when inspected macroscopically. In the case of 3 rabbits the difference was confirmed by freeing the cerebral hemispheres and weighing them. The hemisphere of the ligated side weighed 86–94 per cent of that of the non-ligated side.

**Discussion**

There are very few descriptions in the literature of intracranial arterial aneurysms in animals. Köppen mentioned 1 aneurysm in a colt, Ask-Upmark and Ingvar in a colt, Ask-Upmark and Ingvar in a
llama, and Hassler\textsuperscript{7} in a cow. Aneurysmal lesions of the cerebral arteries have been produced experimentally in dogs by White \textit{et al.},\textsuperscript{18} who applied corrosive agents through a temporal flap directly onto the walls of the arteries of the circle of Willis. This method for producing aneurysms is not to be compared with the mechanism by which the saccular, berry aneurysms arise in human cerebral arteries. The aneurysmal lesions found in the present investigation may, however, resemble the saccular aneurysms of the human cerebral arteries as regards their mode of development.

The findings of the present investigation also throw some light on the origins of saccular aneurysms in man. Thus, support is given to the theory that hydraulic imbalance (in the form of anomalies of the circle of Willis) plays a considerable role in their occurrence\textsuperscript{3,6,7,14,17}.

The value of carotid ligation in the treatment of saccular aneurysms in various locations has been the subject of much discussion in the literature. It is clear from the present investigation that carotid ligation includes a risk that previously has not been calculated.

The changes found in the defects of the media and in the physiological cushions of the intima following carotid ligation, are in accordance with the author's theory\textsuperscript{7,8} that the streaming blood moulds the arterial wall and determines the location and size of the medial defects and of the intimal cushions. In the previous investigation, the author found that the defects of the media occur regularly at that part of the congenitally weak line of junction between main trunk and branch where the streaming blood is forced to change direction, whereas the cushions of the intima lie in those parts of the branching point that are sheltered from the main blood stream.

When this experiment was planned, it was expected that a general change in the histological structure of the cerebral arterial wall would arise on the ligated side as a result of the reduction in the pulse-wave amplitudes distal to the ligature. In this connection two factors were taken into consideration. Firstly, it has been assumed\textsuperscript{1,19} that the lamellar arrangement of the cerebral arterial wall in which all elastic tissue is concentrated in the thick, compact internal elastic lamella, and all the smooth muscle in the media, has a damping function on the pulse-wave trans-

![Fig. 4. Transverse sections through the posterior communicating artery of: (A) the side of the ligation; (B) the opposite side. The greater calibre in (A) is accompanied by a hypertrophy of the tunica media. $\times150$.](image-url)
mission to the sensitive brain parenchyma. If there are only very weak pulsations to damp, the lamellar arrangement might be unnecessary. Secondly, the elastic-tissue content of the arterial wall is thought to depend upon the strength of the pulsations of the wall, and it is noteworthy that a high elastic-tissue content is found regularly in arteries experiencing strong pulsations (elastic arteries). A decrease in the elastic-tissue content of the cerebral arteries distal to the ligation was therefore to be expected. No changes were detected, however, and it is possible that the reduction in the amplitude of the pulsations was too small to be significant.

The finding that the posterior communicating artery on the side of the carotid ligation increases in calibre suggests that developments such as stenosis of the internal carotid artery may cause variations in the calibre of the arteries of the circle of Willis.

The anastomoses of the cerebral arteries and their role in preventing cerebral vascular disease have gained interest during recent years. The findings reported above suggest that the ability to develop anastomoses between the internal and the external carotid systems is greatest in young, growing individuals, and that it takes a comparatively long time (some months at least) before these anastomoses attain their maximum development following ligation of the carotid artery. Embolic or thrombotic occlusion of the internal carotid artery necessitates a more rapid use of the anastomoses.

Summary

In the rabbit, ligation of the internal carotid artery in the neck causes:

1. Structural changes in the walls of the arteries of the circle of Willis, probably resulting from the change in the direction of blood flow. An increase was observed in the size of the defects of the media which occur at the points exposed to the increased hemo-dynamic stress caused by the change in flow. In 6 cases, the defects had a bulging aneurysmal character. The physiological cushions of the intima were altered structurally in accordance with the author's theory which suggests that they should be located at those portions of the branching points that are sheltered from the main blood stream.

2. Increase on the ligated side in the calibre of the posterior communicating, ophthalmic, anterior meningeal, and middle meningeal arteries. The increase was observed to be greater in younger individuals and more pronounced 5 months after ligation as compared with 1 month.

3. Increase in the calibre of the opposite internal carotid artery.

4. A probable decrease in the cerebral hemisphere on the ligated side when the operation is performed at an early age.

References

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