Editorial

The Pathogenesis of Watershed Infarcts in the Brain

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WATERSHED INFARCTS are ischemic lesions which are situated along the border zones between the territories of two major arteries, for example the anterior and middle or the middle and posterior cerebral arteries (fig. 1). They may also be located between the territories of the major cerebellar arteries and they have even been described between the territories of the small arteries in the basal ganglia. However, the exact nature of the latter lesions is more uncertain. The infarcts may be pale or hemorrhagic or mixed but generally the hemorrhagic component is not prominent.

Altogether, approximately 10% of all brain infarcts are watershed lesions. Similar infarcts are also found in other organs, such as the heart and the kidneys, but they are more easily recognized in the brain because of the well defined course and extent of the cerebral arteries.

The mechanisms whereby watershed infarcts develop have been debated for many years and they have been variously ascribed to cerebral thromboangiitis obliterans, episodes of systemic hypotension, carotid occlusions and to microembolism. It has now been convincingly shown that both hypotension and microembolism may cause such lesions. However, in some cases, particularly in those with a progressive or stepwise clinical course, the mechanism still remains uncertain.

Watershed Infarcts Caused by Hypotension

A sharp drop in the systemic blood pressure is the most frequent cause of watershed infarcts. Apparently, the reduction in the blood flow becomes most severe in the terminal areas of the vascular fields. However, this is not the whole explanation because unpredictable combinations of partial uni-and bilateral infarcts may occur. The most striking and most frequent location is the territory between the fields of the anterior and middle cerebral arteries. Sometimes there may be a diffuse nerve cell loss in the cortex in addition to the localized infarcts but the hippocampus appears to be remarkably resistant.

The watershed infarcts caused by hypotension are rarely grossly hemorrhagic. This is somewhat unexpected, since the circulation obviously becomes re-established after the initial ischemic damage to the vascular endothelium. It is also remarkable, and of relevance to certain findings discussed below, that the small leptomeningeal vessels overlying the infarcts rarely become occluded by secondary thrombosis.

Watershed Infarcts Caused by Microemboli

It has often been speculated that the platelet aggregates which so frequently block the small leptomeningeal arteries over watershed infarcts are microemboli and thus the cause of the infarcts rather than secondary events. However, secondary thrombi formed in situ may have a similar appearance and it has therefore been difficult to distinguish between emboli and thrombi in this location.

It has now been shown in a considerable number of cases that showers of cholesterol crystals or of tumor emboli can block the vessels in these areas and cause watershed infarcts. Although admittedly rare causes, these examples of unusual embolic material prove beyond doubt that particles of a certain size may lodge preferentially in the watershed areas and cause infarcts in the underlying brain. Generally, emboli tend to pass as far distally as their size permits along the superficial vascular tree, and they rarely follow the sharp angles of the branches passing to the deeper sites of the brain. Presumably, the microemboli to the watershed areas are extreme examples of this general rule.

Watershed Infarcts Caused by Carotid Occlusions

It has been known for many years that thrombi at the bifurcation of the carotid artery in the neck may cause watershed infarcts between the territories of the anterior and the middle cerebral arteries, and more rarely, between the middle and posterior cerebral arteries. Frequently, these cases present clinically with either transitory ischemic attacks or a stepwise type of development, or with evenly increasing clinical symptoms. Several authors have also commented upon the frequent occurrence of platelet aggregates in the overlying leptomeningeal vessels.

The watershed infarcts in carotid occlusions have mostly been considered to be due to a reduced blood flow analogous to the situation following systemic hypotension and the occluded leptomeningeal vessels a
result of "stagnation thrombi." It is also clear that showers of microemboli may lodge preferentially in these areas and cause infarcts in the underlying brain. This is the most frequent cause. It is also clear that showers of microemboli may lodge preferentially in these areas and cause infarcts in the underlying brain. This is the most likely explanation for the watershed infarcts in cases of carotid thrombosis.

Finally, there are examples of bilateral progressive watershed infarcts with small vessel occlusions, in which both episodes of hypotension and sources of microemboli are lacking. Clinically, these cases often have a stepwise or evenly progressive course. There is evidence that at least some of these cases are caused by hematogenous disorders with abnormal platelet aggregation resulting in clogging of the small vessels in the watershed areas of the brain and in many other organs.

Watershed Infarcts of Unknown Cause

In this group of infarcts there are neither episodes of hypotension nor sources of microemboli which can explain the lesions. Clinically, these cases often show a stepwise or gradually increasing course. The lesions are composed of multiple small and partly confluent bilateral infarcts which are most prominent in the areas between the anterior and middle cerebral arteries. The infarcts frequently give the cortex an appearance of "granular atrophy."

Many leptomeningeal arteries over the infarcts are occluded by a material which shows all transitional stages from recent platelet aggregates to completely organized fibrous occlusions. These observations thus indicate an ongoing process within the watershed zones.

As mentioned above, such cases were originally interpreted as instances of cerebral thromboangiitis obliterans. This interpretation was convincingly refuted many years ago by Fisher and later the infarcts have been mostly considered due to a combination of reduced cardiac output and stenosing cerebral athroscle-
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