The Relation between Retinal and Cerebral Vascular Reactivity in Normal and Arteriosclerotic Subjects

By J. B. Hickam, M.D., J. F. Schieve, M.D., and W. P. Wilson, M.D.

It has been found that retinal arterial reactivity to oxygen is diminished in persons with retinal arteriosclerosis, and that cerebral blood flow and the increment in cerebral flow upon inhalation of carbon dioxide are diminished in persons with cerebral arteriosclerosis. The present study demonstrates that there is a significant positive correlation between retinal arterial reactivity on the one hand, and cerebral blood flow and reactivity, on the other. This finding is taken to mean that arteriosclerosis severe enough to affect measurements of this sort is apt to involve retinal and cerebral vessels together.

Because of their unique accessibility, the retinal vessels are routinely inspected during the course of a physical examination, and, from their condition, inferences are often made as to the condition of vessels of similar size in other body regions. It is an important clinical question whether such inferences have validity. On the basis of histologic examination, Alpers, Forster, and Herbut\(^1\) have concluded that the relation between cerebral and retinal arteriosclerosis is not particularly close. It is now possible to assess the relation between disease of vessels in these two regions by functional tests which measure the reactivity of the vessels in the fundus and brain.

It has been found that persons with retinal arteriosclerosis have impairment of the constrictor response shown by normal retinal arteries when the subject inhales oxygen.\(^2\) It has also been found that persons with cerebral arteriosclerosis not only have a diminished cerebral blood flow,\(^3\) \(^4\) but also have less than the normal increase in cerebral flow in response to inhalation of carbon dioxide.\(^4\) It is the purpose of the present study to determine whether retinal and cerebral vascular disease, as determined by measurements of this kind, coexist with significant frequency. To this end, measurements of retinal vascular reactivity to oxygen, and of cerebral blood flow and cerebral vascular reactivity to carbon dioxide have been made together in a group which includes normal persons, persons with overt cerebral vascular disease, and persons having illnesses commonly associated with generalized arteriosclerosis.

Methods

Retinal vascular reactivity was determined, as previously described,\(^1\) from measurements made on fundus photographs, and was expressed as the average per cent decrease in visible vessel diameter which resulted when the subject changed from breathing air to breathing tank oxygen. The measurement was made separately for arteries and veins. Cerebral blood flow was measured by the method of Kety and Schmidt\(^4\) as modified by Scheinberg and Stead.\(^5\) The increase in cerebral blood flow ("cerebral vascular reactivity") after five minutes' administration of 5 per cent carbon dioxide or 7 per cent carbon dioxide was estimated from the decrease in cerebral arteriovenous oxygen difference, as described by Schieve and Wilson.\(^6\)

Results

1. Correlation between Retinal Vascular Reactivity and Cerebral Blood Flow

Since the cerebral blood flow is known to be diminished in diffuse cerebral vascular disease, a test was made of the correlation between...
resting cerebral blood flow and the retinal vascular reactivity to oxygen. This was done in 31 subjects. These subjects included normal persons over a wide age range, persons who had had cerebral vascular accidents, hypertensives, diabetics, patients with senile dementia, and others. The mean cerebral blood flow of the group was 53.1 (S.D. 15.2) cc. per 100 Gm. per minute (mean normal: 59, S.D. 11); the retinal arterial reactivity was 9.5 per cent, standard deviation 5.8 (mean normal 11.5, 4.2); and the venous reactivity was 15.8 per cent, standard deviation 7.2 (mean normal 14.0, S.D. 5.6).

The pertinent results are presented graphically in figure 1, which relates retinal arterial reactivity to cerebral blood flow. There is a significant positive correlation between the two (r = .465, t = 2.820, p < .01). It will be noted from figure 1 that there are a number of instances in which reactivity and flow are not closely related, some persons having a poor reactivity but good flow, while some show good reactivity but a subnormal flow.

The correlation between retinal venous reactivity and cerebral blood flow is not at a significant level.

2. Correlation between Retinal Vascular Reactivity to Oxygen and Increase in Cerebral Blood Flow in Response to Carbon Dioxide

This relationship is of interest because it compares a function of motility in retinal vessels with a function of motility in cerebral vessels. Schieve and Wilson have shown that persons with cerebral vascular disease have significantly less increase in cerebral blood flow on breathing carbon dioxide than do normal persons.

![Fig. 1. Correlation between retinal arterial reactivity and resting cerebral blood flow in 31 subjects. Correlation coefficient = .465, t = 2.820, p < .01. The regression of reactivity on flow is Y = .18X. The standard deviation from regression is 5.3.](image1)

![Fig. 2. Correlation between retinal arterial reactivity to oxygen and increase in cerebral blood flow on inhalation of 5 per cent carbon dioxide in 21 subjects. The correlation is highly significant (r = .632, t = 3.550, p < .01). The regression of reactivity on flow change is Y = .234X + 1.8. The standard deviation is 4.2.](image2)

![Fig. 3. Correlation between retinal arterial reactivity to oxygen and increase in cerebral blood flow on inhalation of 7 per cent CO₂ in 22 subjects. The correlation is significant (r = .463, t = 2.330, .02 < p < .05), but not so good as for 5 per cent carbon dioxide. The regression of reactivity on flow change is Y = .13X + 1.7.](image3)
7.4 per cent. For the group on 7 per cent carbon dioxide, the mean increase in flow was 59 cc. (mean normal 70 cc.), and the retinal arterial reactivity was 9.4 per cent.

The data on retinal arterial reactivity and cerebral blood flow increase on 5 per cent carbon dioxide are presented in figure 2. There is a highly significant positive correlation \( (r = .632, t = 3.550, p < .01) \). Venous reactivity was also significantly correlated with flow change, but less closely \( (r = .489, t = 2.490, .01 < p < .02) \).

The data on arterial reactivity and cerebral flow change in the group receiving 7 per cent carbon dioxide are presented in figure 3. The correlation is again significant \( (r = .463, t = 2.330, .02 < p < .05) \), but not so highly significant as in the group receiving 5 per cent carbon dioxide. Venous reactivity was not significantly correlated with flow change.

In the over-all picture, retinal arterial reactivity is significantly correlated with the resting cerebral blood flow and with the increase in flow which results from the inhalation of carbon dioxide. The closest correlation, and one which is statistically highly significant, is that between retinal arterial reactivity and the increase in cerebral flow on 5 per cent carbon dioxide. Retinal venous reactivity, in general, correlates poorly with these functions of the cerebral circulation.

**DISCUSSION**

Persons with retinal arteriosclerosis have a decreased retinal arterial reactivity.\(^1\) Persons with cerebral arteriosclerosis have a decreased cerebral blood flow and cerebral vascular reactivity.\(^3,4\) In a group which includes normal and arteriosclerotic persons, retinal arterial reactivity is significantly correlated with cerebral flow and reactivity. It appears from this that arteriosclerosis which is advanced enough to affect these measurements is apt to involve both retinal and cerebral vessels. There are certainly exceptions to this generalization. These are apparent on inspection of the figures.

Inspection of figures 2 and 3 suggests the possibility of making further generalizations as to what the retinal arterial reactivity of a subject may mean in terms of cerebral vascular reactivity. A markedly reduced retinal arterial reactivity suggests, but certainly does not guarantee, a subnormal cerebral vascular reactivity. On the other hand, an average or above average retinal arterial reactivity is quite apt to be associated with a cerebral vascular reactivity within the normal range.

It is concluded that retinal arterial reactivity has extrapolative significance in terms of the cerebral circulation.

**SUMMARY AND CONCLUSIONS**

1. Parallel measurements of retinal arterial reactivity to oxygen, on the one hand, and cerebral blood flow and cerebral vascular reactivity to carbon dioxide, on the other, have been made in normal and arteriosclerotic subjects.

2. Retinal arterial reactivity is significantly correlated with cerebral flow and reactivity.

3. This finding is taken to mean that arteriosclerosis severe enough to affect measurements of this sort is apt to involve retinal and cerebral vessels together. There are definite exceptions to this generalization.

**SUMARIO ESPAÑOL**

Se ha encontrado que la reactividad arterial retinal al oxígeno está disminuida en personas con arteriosclerosis retinal y que la circulación cerebral al inhalar bario disminuyó en personas con arteriosclerosis cerebral. El presente estudio demuestra que existe una correlación positiva significativa entre la reactividad arterial retinal en un lado, y la reactividad de la circulación cerebral en el otro. Este hallazgo significa que arteriosclerosis suficientemente severa para afectar determinaciones de esta naturaleza es capaz de implicar los vasos retinale y cerebrales a la vez.

**REFERENCES**

HICKAM, SCHIEVE AND WILSON


The Relation between Retinal and Cerebral Vascular Reactivity in Normal and Arteriosclerotic Subjects

J. B. HICKAM, J. F. SCHIEVE and W. P. WILSON

Circulation. 1953;7:84-87
doi: 10.1161/01.CIR.7.1.84

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1953 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/7/1/84

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/