Large Virchow-Robin Spaces:
MR-Clinical Correlation

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High-field MR scans frequently show Virchow-Robin spaces, which conform to the path of the penetrating arteries as they enter either the basal ganglia or the cortical gray matter over the high convexities. A retrospective review of 816 MR scans was undertaken to determine the clinical significance and associations (if any) of this finding. The Virchow-Robin spaces were graded, as were the nonspecific white-matter lesions. The presence of atrophy, infarction, hydrocephalus, and miscellaneous disease was noted. Large Virchow-Robin spaces were identified in 314 cases. A study sample was created consisting of a positive group containing all the larger grade 2 and 3 Virchow-Robin spaces (67 patients) and a negative or control group of 109 randomly selected patients from the original 502 who did not have large Virchow-Robin spaces. The charts of this study sample were reviewed and the following patient variables were noted: age, gender, incidental white-matter lesions, infarction, dementia, hypertension, and atrophy. For each variable, the proportion of patients who were positive for that variable was calculated for each of the two groups and compared across groups by using a Fisher exact test. Multiple logistic regression analysis was used to determine whether any of these variables were jointly associated with being "positive" or "negative" for large Virchow-Robin spaces. Some variables were strongly associated with being positive for large Virchow-Robin spaces: age, hypertension, dementia, and incidental white-matter lesions. Logistic regression analysis revealed that when all of these variables are considered jointly, only age remains significant.

In conclusion, large Virchow-Robin spaces are another phenomenon of the aging brain. Factors such as hypertension, dementia, and incidental white-matter lesions were significantly associated with large Virchow-Robin spaces, but were believed to accompany the aging process rather than represent independent variables.

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High-field MR scans routinely demonstrate small foci of CSF signal on all pulse sequences about the base of the brain. These lesions conform to the path of the lenticulostriate arteries as they enter the basal ganglia through the anterior perforated substance and represent large Virchow-Robin spaces, which accompany the vessel as it penetrates the brain from the subarachnoid space. Occasionally, these perforations have been seen in the high-convexity gray matter extending into the centrum semiovale, where they follow the course of the penetrating cortical arteries. A retrospective review of 816 MR scans was undertaken to determine the clinical significance and associations, if any, of this anatomy.

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Materials and Methods

All outpatients who had an MR scan of the brain between October 1986 and August 1987 on a 1.5-T General Electric Signa unit were retrospectively reviewed for the presence or absence of large Virchow-Robin spaces. The routine examination consisted of three spin-echo sequences, all done with a 256 × 256 matrix and one excitation: (1) axial images, 600–800/20 (TR/TE), with a 5-mm section thickness and 5-mm gap; (2) axial multiecho images,

2000/40, 80, with a 5-mm section thickness and 2.5-mm gap; and (3) sagittal images, 800/20, with a 5-mm section thickness and 5-mm gap.

By definition, a Virchow-Robin space had to be isointense relative to CSF on all pulse sequences, conform to the path of penetrating arteries, and have no mass effect. The location of these spaces was recorded as lenticulostriate and/or high convexity. The number and size of the Virchow-Robin spaces were used to grade their severity. As a rule, mild grade 1 spaces were under 2 mm in diameter, moderate grade 2 spaces were 2–3 mm, and marked grade 3 spaces were over 3 mm. The size of the spaces was measured with calipers on the films, and then the measurement in millimeters was obtained from the 5-cm reference scale found on each image. However, a large number of smaller spaces (four or more) would result in an upgrade to the next level. The presence of both cortical and lacunar infarcts, atrophy, and miscellaneous diseases was noted. Atrophy was evaluated qualitatively by two independent observers and not recorded if both observers believed it was appropriate for the patient's age. Only when the atrophy was greater than expected for the patient's age was it recorded. If the two observers did not agree, the final determination was made by a third neuroradiologist.

Nonspecific white-matter lesions seen only on the long TR images were graded on a scale of 0 to 3 as follows: 0.0 = no lesions, 0.5 = less than three punctate lesions, 1.0 = more than three punctate lesions, 1.5 = more than seven punctate lesions, 2.0 = patchy focal lesions, and 3.0 = coalescent lesions. Patients with a known cause of white-matter disease—that is, those with multiple sclerosis or previous radiation therapy—were not considered to have nonspecific white-matter lesions.

A study sample consisting of all 67 patients with "larger" (grades 2 and 3) Virchow-Robin spaces was selected from the 314 patients with Virchow-Robin spaces; this group was defined as "positive." The "negative" group (i.e., controls) consisted of a random sample of 109 patients from among the 502 patients who were negative for Virchow-Robin spaces. The random selection was obtained by alphabetizing the 502 patients by name and taking the first 109 patients beginning with the letter A. Our statistician calculated that at least 100 cases were required for the sample size to be statistically significant.

The charts from the patients in the study sample were reviewed for age, gender, clinical history of infarction, dementia, and hypertension. The presence of dementia was determined by the examining neurologist who referred the patient for MR. At our institution, neurologists define dementia as a loss of higher integrative faculties such that it interferes with the activities of daily living. A patient was considered to be hypertensive if he or she was being treated with medication and/or if diastolic pressures of over 90 mm Hg had been measured on two separate occasions. Finally, several patient variables were recorded for statistical analysis: age, gender, incidental white-matter lesions, infarction (on MR), dementia, hypertension, and atrophy (greater than expected for age only). For each variable, the proportion of patients who were positive for that variable (e.g., positive for hypertension) was calculated for each of the two groups and compared across groups by using a Fisher exact test. Multiple logistic regression analysis was used to determine whether any of these variables were jointly associated with being positive or negative for large Virchow-Robin spaces. The Mann-Whitney test was used to compare the age distributions across groups.

A second phase of the analysis was to define the positive patients as either high convexity only, lenticulostriate only, or both high convexity and lenticulostriate and to determine whether membership in these groups was associated with any of the clinical or demographic factors. These analyses were also carried out by using the Fisher exact test. All results were reported as statistically significant if $p < .05$.

Results

Large Virchow-Robin spaces were identified in 314 patients. The age distribution of these patients is given in Figure 1, where it is compared with the age distribution of the 502 cases negative for Virchow-Robin spaces. Note that it is in the two older groups that the percentage of positives exceeds that of the negatives. More specifically, it is in the 61–80 age group that the percentage of patients positive for Virchow-Robin spaces is significantly greater than the percentage of those who are negative.

Table 1 illustrates the prevalence of the various grades of Virchow-Robin spaces found in each age group. In general, Virchow-Robin spaces increased with increasing age, but larger Virchow-Robin spaces (grades 2 and 3) had a much stronger correlation with age while the milder grade 1 spaces were more ubiquitous.

Lenticulostriate Virchow-Robin spaces were common and mildly age-related, while high-convexity spaces were rarer and had a much stronger correlation with age, as illustrated in Figures 2–4. Two hundred eighty-five patients (35%) had lenticulostriate spaces, 102 (13%) had high-convexity spaces, and 74 (9%) had both.

In the study sample in which only the age distribution of the larger Virchow-Robin spaces (grades 2 and 3) was analyzed and compared with the control group, the correlation with age was further strengthened (Fig. 5).

Figure 6 shows that patients who were positive for Virchow-Robin spaces were more likely to have nonspecific white-

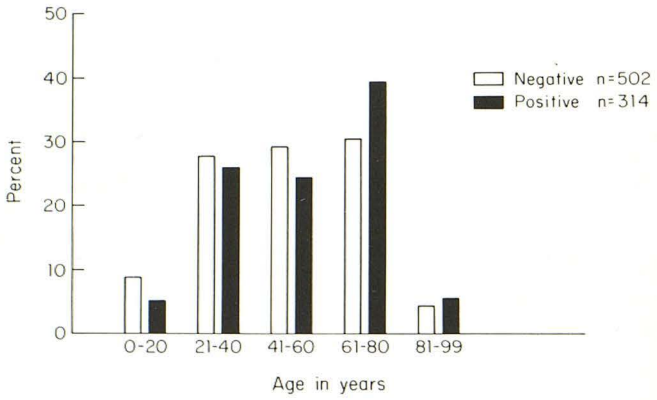


Fig. 1.—Age distribution of the 502 patients without Virchow-Robin spaces and the 314 patients with large Virchow-Robin spaces.

TABLE 1: Prevalence of Grades 1–3 Virchow-Robin Spaces by Age

Age	No. of Cases	% by Grade		
		Grade 1	Grades 2 & 3	Total
<20	60	23	3	26
21–40	220	33	4	37
41–60	222	28	6	34
61–80	276	33	12	45
>80	38	18	27	45

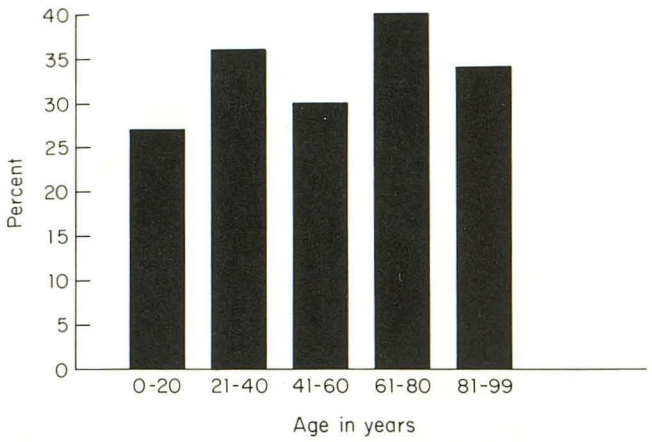


Fig. 2.—Age-specific prevalence of lenticulostriate Virchow-Robin spaces seen on MR.

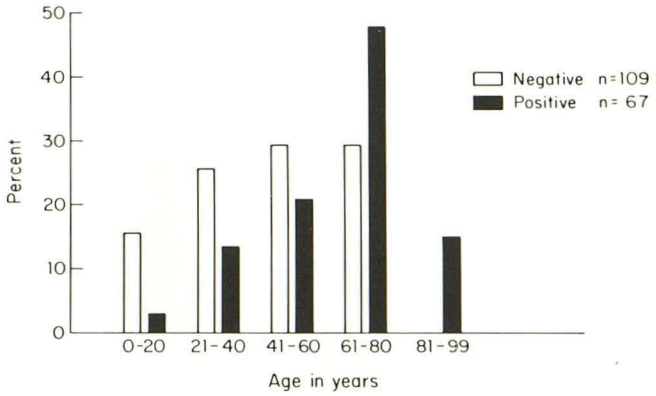


Fig. 5.—Age distribution of patients with large (grades 2 and 3) Virchow-Robin spaces vs controls.

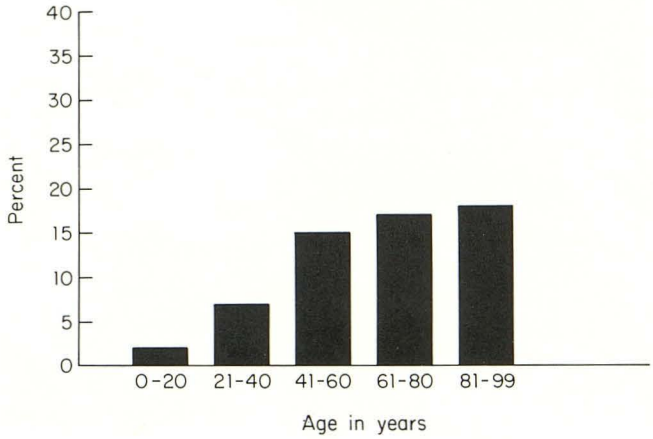


Fig. 3.—Age-specific prevalence of high-convexity Virchow-Robin spaces seen on MR.

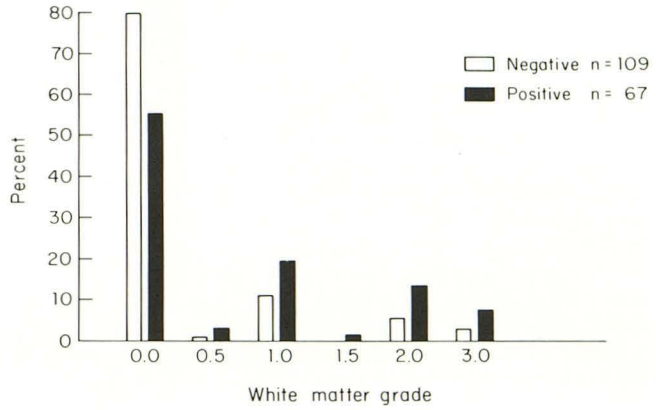


Fig. 6.—Prevalence and severity of white-matter lesions in patients with large (grades 2 and 3) Virchow-Robin spaces vs controls.

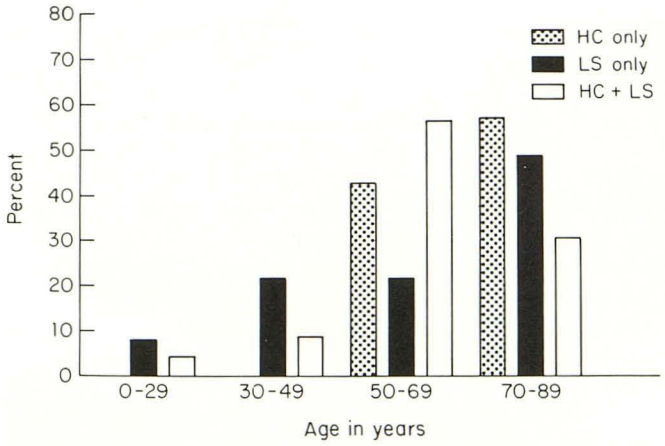


Fig. 4.—Age-specific prevalence of type of Virchow-Robin space among 67 large Virchow-Robin spaces (grades 2 and 3). HC = high convexity; LS = lenticulostriate.

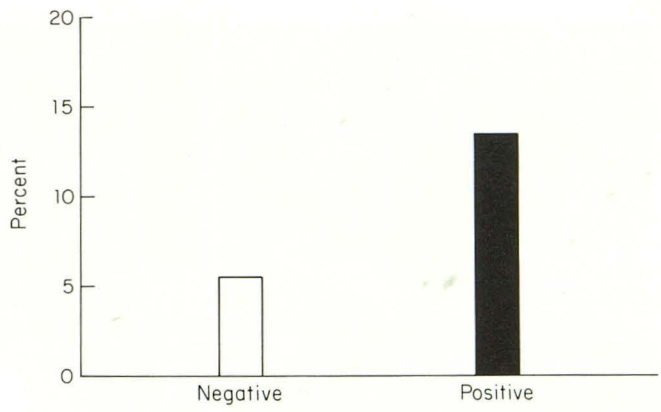


Fig. 7.—Prevalence of dementia in patients with large (grades 2 and 3) Virchow-Robin spaces vs controls.

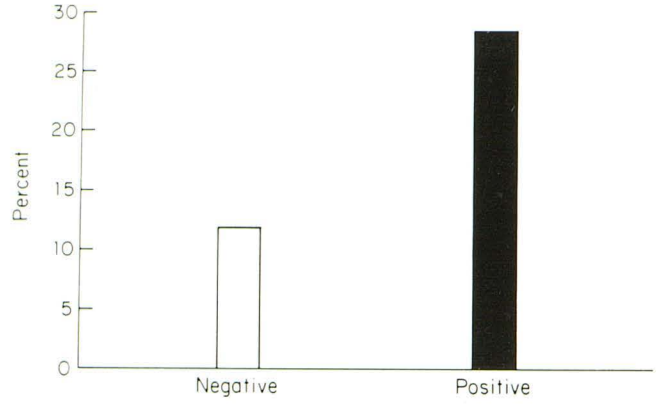


Fig. 8.—Prevalence of hypertension in patients with large (grades 2 and 3) Virchow-Robin spaces vs controls.

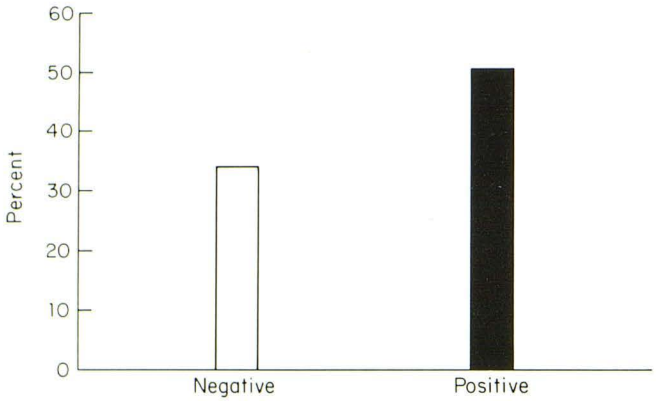


Fig. 9.—Prevalence of male patients with large (grades 2 and 3) Virchow-Robin spaces vs controls.

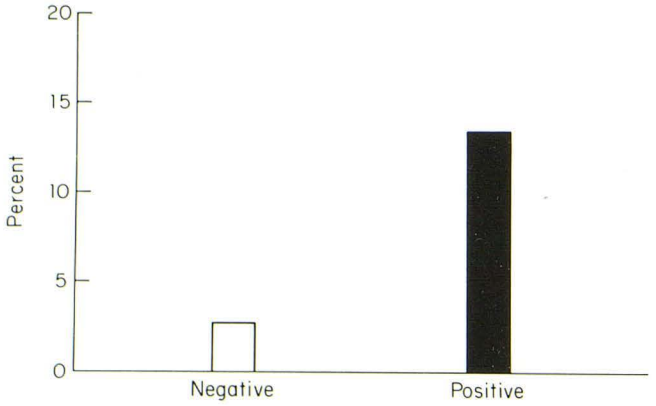


Fig. 10.—Prevalence of stroke in patients with large (grades 2 and 3) Virchow-Robin spaces vs controls.

matter disease (grades 0.5–3.0) than were patients who were negative for Virchow-Robin spaces.

Some variables were significantly associated with being positive for large Virchow-Robin spaces: age ($p = .0001$), hypertension ($p = .009$), dementia ($p = .011$), and incidental

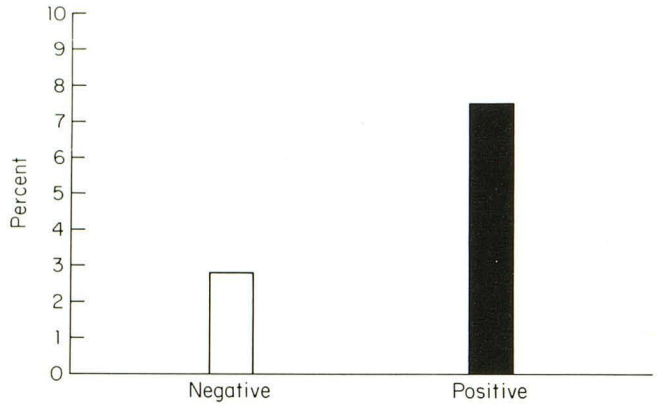


Fig. 11.—Prevalence of atrophy in patients with large (grades 2 and 3) Virchow-Robin spaces vs controls.

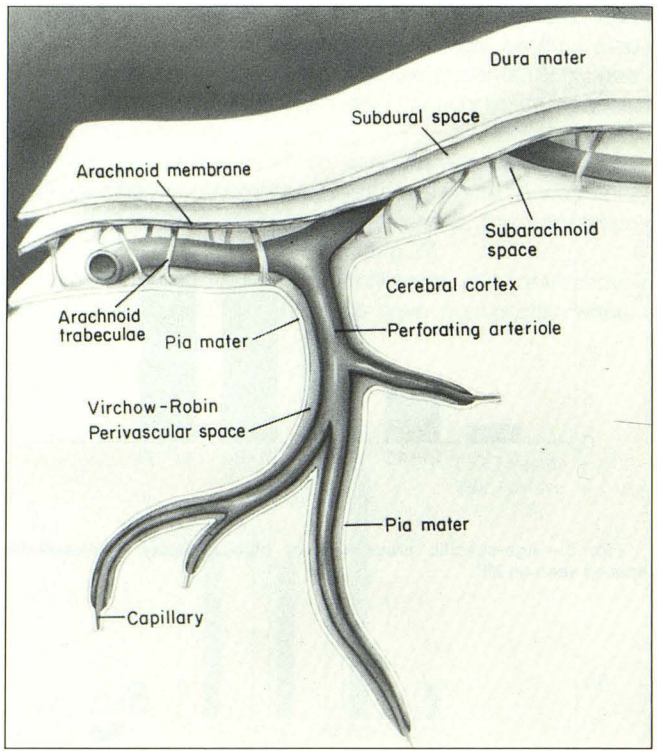


Fig. 12.—Simplified illustration of perivascular space of Virchow-Robin.

white-matter lesions ($p = .0001$). Gender (more males than females) also was mildly significant ($p = .04$). Although stroke and atrophy occurred with higher frequencies in the positive group, these results were not statistically significant (Figs. 6–11). All the cortical infarctions had a clinical history of ictus while lacunar infarcts had a history of ictus in only half the cases.

Owing to small numbers, stroke and atrophy were excluded from the logistic regression analysis. Logistic regression was carried out on age, gender, hypertension, dementia, and white matter. The analysis revealed that, when all these clinical variables were considered jointly, only age remained significant ($p = .0002$).

The second analysis showed no significant association of the high convexity/lenticulostriate grouping with any of the variables, except for a weak association with hypertension ($p = .05$); patients with both high convexity and lenticulostriate Virchow-Robin spaces were more likely to have a history of hypertension.

Discussion

In the past, the perivascular space has been the exclusive domain of the anatomists and pathologists, as no imaging technique had the resolution required to visualize such anatomic detail. While Pestalozzi in 1849 (cited in [1]) was probably the first to describe a perivascular space, what has become known as a Virchow-Robin space was described in 1851 by Virchow [2], a German pathologist, as a subadventitial space that was contiguous around the capillaries. In 1859, Robin [3], a French anatomist, described a space he regarded as intraadventitial and closed. Today, the eponym refers to the extension of the subarachnoid space, which accompanies the vessel penetrating the cerebral cortex to the level of the capillaries (Fig. 12) [1, 4]. While late-generation CT scanners have enabled the visualization of pathologic processes dilating the Virchow-Robin spaces [5], it is only with the advent of high-field MR imagers and their greater resolution that presumably "empty" CSF-filled Virchow-Robin spaces have been routinely visualized [6, 7].

MR scans obtained at 1.5 T routinely demonstrate small foci of CSF signal on all pulse sequences on either side of the anterior commissure at the level of the inferior one third of the basal ganglia; that is, in the anterior perforated substance (Figs. 13 and 14). These Virchow-Robin spaces follow the path of the lenticulostriate arteries as they enter the basal ganglia through the anterior perforated substance (Figs. 15 and 16). Infrequently, Virchow-Robin spaces are seen in the high-convexity gray matter extending into the centrum semi-

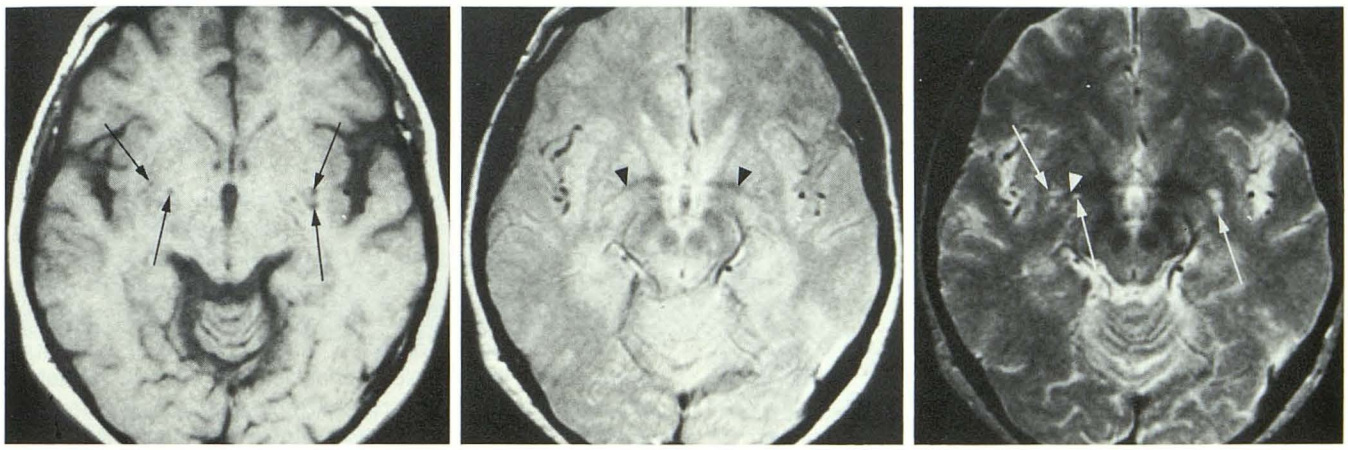


Fig. 13.—62-year-old woman with vertigo.
***A–C*, 800/20 (*A*), 2000/40 (*B*), and 2000/80 (*C*) images. Large grade 3 perivascular spaces (*arrows*) are seen on either side of anterior commissure (*arrowheads*) and are isointense relative to CSF on all pulse sequences.**

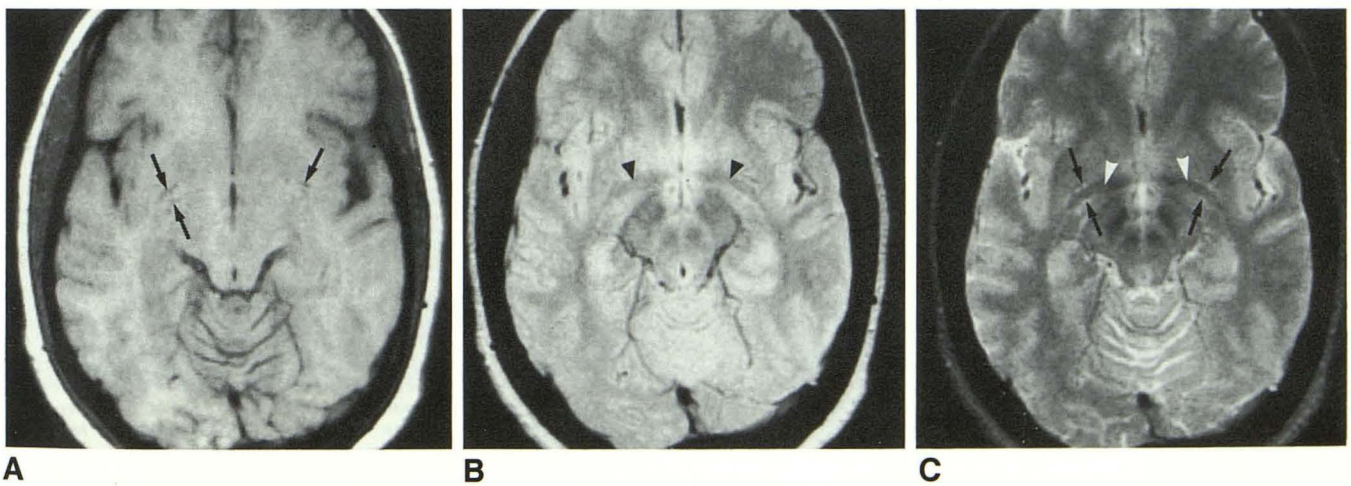


Fig. 14.—38-year-old woman with headache.
***A–C*, 800/20 (*A*), 2000/40 (*B*), and 2000/80 (*C*) images. Mild grade 1 spaces (*arrows*) are seen on either side of anterior commissure (*arrowheads*).**

ovale (Figs. 17 and 18), where they follow the course of the penetrating cortical arterioles (Fig. 19). The artery contained within the large Virchow-Robin space is not identified on MR because the associated perivascular space is so much larger and the size of the vessel itself (usually 0.4 mm and under) is beyond the limits of the scanner's resolution (0.93 mm with a 5-mm slice and 24-in. [61-cm] field of view) (Figs. 16B and 19).

Occasionally, it is difficult to differentiate a lacunar infarct from a large perivascular space, but in our experience and others [6–8] infarctions occur in the upper two thirds of the basal ganglia and are usually not of CSF intensity on all pulse sequences. Infarcts tend to be hyperintense or have hyperintense edges on long TR/short TE images and they tend to be larger, usually measuring 5 mm in diameter or more. Perivascular spaces are far more symmetric and bilateral (85% of our cases) than lacunae as well. A new classification of cerebral lacunae was proposed in the pathologic literature by Poirier and Derouesne [9]. Type I lacunae refer to old, small infarcts; type II lacunae refer to old, small hemorrhages; and type III lacunae refer to dilated perivascular spaces. The authors specifically described a type IIIC lacuna corresponding to perivascular dilatation at the entrance of a perforating artery into the lenticular nucleus. This clearly corresponds to our dilated Virchow-Robin spaces about the lenticulostriate arteries.

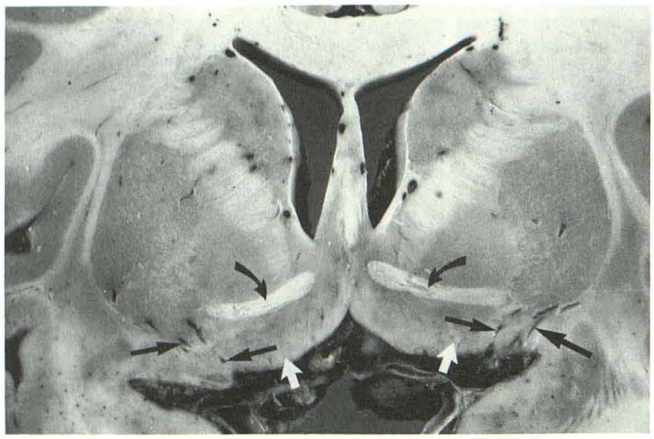
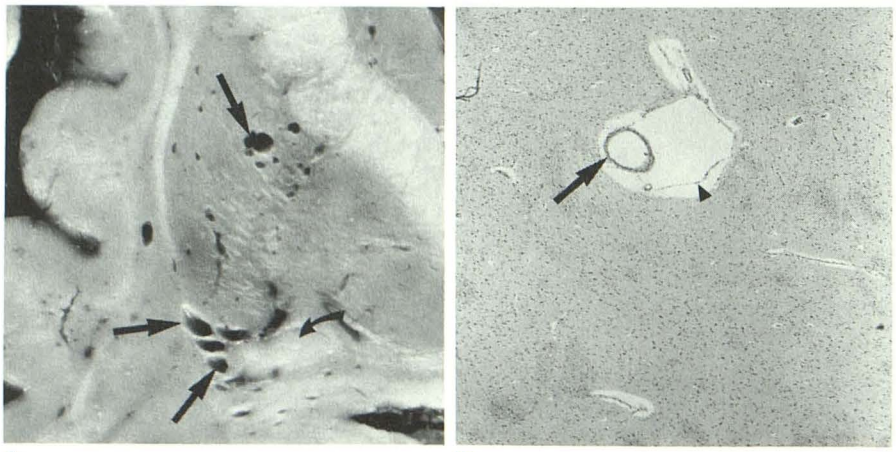


Fig. 15.—Gross specimen sectioned in coronal plane. Lenticulostriate arteries (*straight black arrows*) are seen passing through anterior perforated substance (*white arrows*) at level of anterior commissure (*curved arrows*). Perivascular spaces are not enlarged.

Our results indicate that small (grade 1) Virchow-Robin spaces are found in all age groups and probably represent normal anatomy. Grade 1 Virchow-Robin spaces were seen in 23% of cases under age 20, in 33% of cases aged 21–40, in 28% of cases aged 41–60, in 33% of cases aged 61–80, and in 18% of cases aged 80 and over (Table 1). High-convexity spaces are less common and much more age-related than lenticulostriate spaces, although both are found with increasing size and frequency with advancing age (Figs. 1–5).

Age, hypertension, dementia, and incidental white-matter lesions were found to be significantly associated with large Virchow-Robin spaces (grades 2 and 3). Infarction and atrophy occurred more frequently with large spaces as well, but the numbers were not statistically significant (Figs. 6–11). Atrophy was noted only if it was not appropriate for the patient's age, so it must be remembered that age in this cohort is also an index of atrophy. The multiple logistic regression analysis revealed that when all the above variables were considered jointly, only age remained significant. The interpretation is that age alone accounts for the differences between groups and that the other variables do not independently distinguish between groups. This result is not surprising, since these clinical variables are so highly correlated with age. Because the Virchow-Robin space is an extension of the subarachnoid space, it should be expected that it would enlarge with age, as the subarachnoid space does elsewhere in the brain. In conclusion, large Virchow-Robin spaces are another phenomenon of the aging brain.



A **B**

Fig. 16.—*A*, Severe dilated Virchow-Robin spaces (*straight arrows*) about anterior commissure (*curved arrow*) in gross specimen sectioned in coronal plane.

***B*, Accompanying histologic section with pial-lined (*arrowhead*) perivascular space. Vessel (*arrow*) measures 0.25 mm in diameter and space measures 1.05 mm (grade 1). MR was performed on this specimen. (H and E, ×4)**

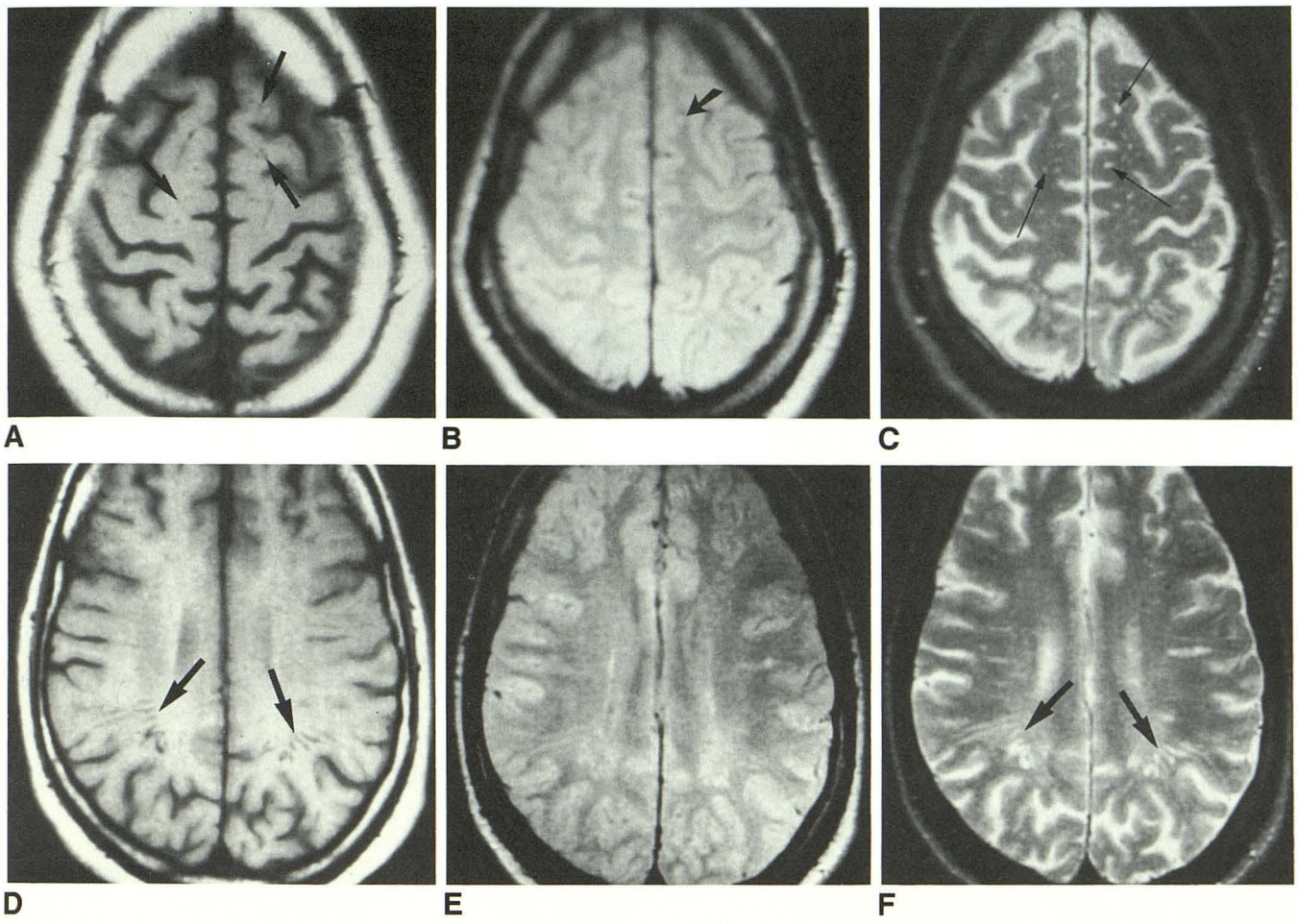


Fig. 17.—61-year-old man with basal ganglia hemorrhage and hypertension.
A–C, 800/20 (*A*), 2000/40 (*B*), and 2000/80 (*C*) images show high-convexity Virchow-Robin spaces perforating cortex (*arrows*).
D–F, 800/20 (*D*), 2000/40 (*E*), and 2000/80 (*F*) images show high-convexity Virchow-Robin spaces extending into periventricular white matter (*arrows*).

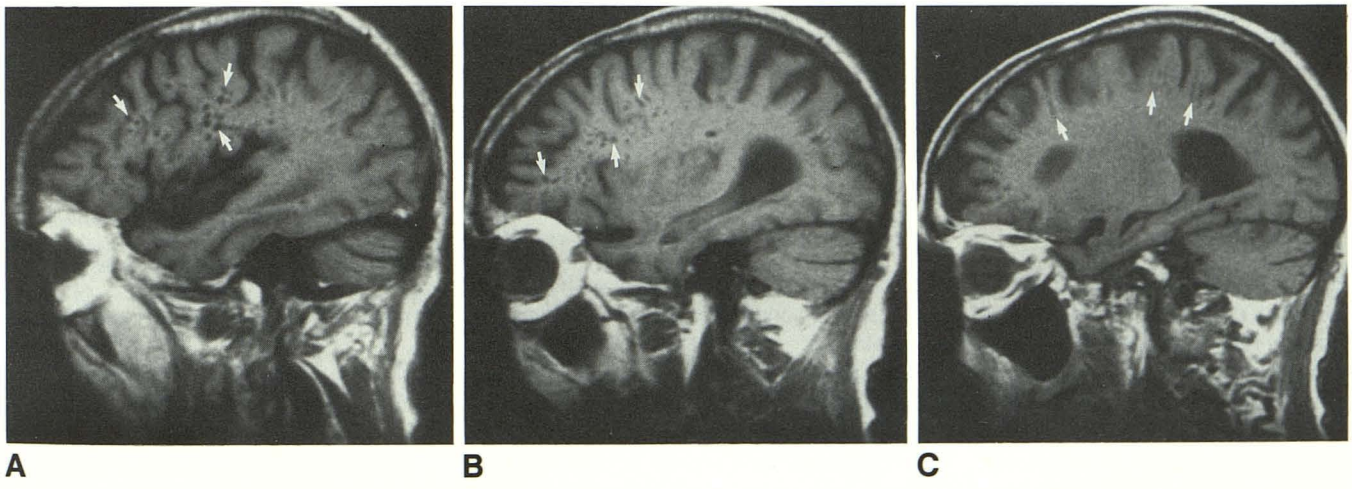


Fig. 18.—83-year-old man with vertebral basilar ischemia.
A–C, Sagittal images (800/20) show high-convexity Virchow-Robin spaces traversing corona radiata (*arrows*) from lateral to medial.

Fig. 19.—Histologic section of high-convexity Virchow-Robin space (*straight arrow*) containing longitudinally sectioned arteriole (*arrowheads*) in centrum semiovale. Note corticomedullary junction (*curved arrow*). MR was not performed in this case. (H and E, ×4)

ACKNOWLEDGMENTS

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