

controls free of A β deposits.² To address the causal relation between cerebral microvasculature with attenuated or degenerated endothelium and amyloidotic lesions, we did quantitative analyses of frontal, temporal, and occipital cortices from 15 prospectively assessed individuals with AD (figure). Our results show that both the number and length of degenerated microvessel profiles were significantly correlated with neocortical A β deposits ($p < 0.001$ for both measures) but there was no apparent relation between the degenerated microvessels and neurofibrillary tangles ($r = 0.13$, $p > 0.05$) or existing pyramidal neurons ($r = 0.06$, $p > 0.05$). The significant correlations were apparent in layers three to five of the neocortex and present in all cortical lobes. As expected, we also noted a weak correlation between the density of A β deposits and neurofibrillary tangles.

We suggest that the vascular changes along with a profound microangiopathy⁴ are concomitant with A β deposition and imply abnormalities in the patency of the brain microvasculature in AD.⁵ The vascular findings imply that neurofibrillary tangles or neurons are unlikely to be primary factors in the degeneration of cerebral vessels.⁵ Our observations may have wider implications on cerebral perfusion and permeability.

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BRCA1 mutations in young women with breast cancer

SIR—Two surveys for germline *BRCA1* mutations in patients with breast cancer provided the first direct estimates of mutation prevalence outside of high-risk families.^{1,2} There were mutations in approximately 10% of patients with breast cancer diagnosed in their twenties and early thirties (similar to previous estimates³). We looked for *BRCA1* mutations in patients with breast and ovarian cancer diagnosed at or before age 35.

Cases were from a population-based cohort of 143 517 radiological technologists.⁴ Of 88 breast and 43 ovarian cancers at or before age 35, lymphocyte DNA was available from 53 women with breast and 17 women with ovarian cancer who gave informed consent for genetic testing. Targeted mutation screening was carried out with allele-specific oligonucleotide assays for 15 *BRCA1* mutations 185delAG, C61G, C64G, 1136insA, 1294del40, 1323delG, 3600del11, 3875del4, 4184del4, R1443X, R1443G, 5256delG, V1713A, 5382insC, and 5438insC.⁵ These include all mutations that have been reported in six of more unrelated women, either published or in the Breast Cancer Information Core database (http://www.nchgr.nih.gov/Intramural_research/Lab_transfer/Bic/). They represent 45% of all unrelated individuals reported with *BRCA1* mutations, although this may be an overestimate due to selective screening for some mutations. We detected 185delAG, 5382insC, and C61G in three women with

breast cancer. Assuming the assays employed in this study detect 45% of all *BRCA1* mutations, then 12.6% of the women with breast cancer in this series may be carriers. The 185delAG mutation was detected in one Jewish woman who did not report any relatives with breast or ovarian cancer. Both of the other mutation carriers reported at least one first or second degree relative with breast cancer. There were no mutations in patients with ovarian cancer.

Our results support evidence that approximately 10% of very-early-onset cases of breast cancer may have germline alterations. Although inadequate for diagnostic purposes, targeted screening may be an efficient research tool. If the distribution of specific *BRCA1* mutations in the general population is similar to that observed thus far in high-risk families and early-onset breast cancer cases, large number of individuals could be screened in this manner to obtain population-based estimates of mutation prevalence.

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The Vellore vibrio watch

SIR—*Vibrio cholerae* O139 is a new pathogen that emerged in the early 1990s in the south Indian peninsula.^{1,2} Within 1 year it had spread to nearly all regions within India and to Bangladesh, Nepal, and other Asian countries.³ From the beginning we have been following its epidemiological behaviour (in our microbiology laboratory) from the numbers of isolations over time and comparing them with those of *V cholerae* O1.^{4,5} In Vellore, O1 vibrios have been endemic for many years, causing summer outbreaks of cholera almost every year, until 1991. In that year a number of clinical cholera cases were due to non-O1 organisms, which surprised us, but we did not investigate this change.¹ In 1992, when the cholera outbreak occurred in September, having missed the summer, *V cholerae* O1 was conspicuous by its absence, and the outbreak was entirely due to the by then newly recognised *V cholerae* serogroup O139.^{1,4}

Subsequent events are summarised here, illustrated in the figure. After the virtual absence of O1 vibrios during 1992–93, they reappeared during the last quarter of 1993, and for several months both O1 and O139 were concurrently prevalent, as reported earlier.⁵ The 1994 summer outbreak of cholera began in May when both organisms were prevalent; thereafter the outbreak was almost entirely due to O139, and it subsided in September. We then concluded that the cholera vibrios had settled their competition; we predicted that subsequent summer outbreaks would be dominated by O139, suspecting that O139 had some survival and spread advantages over O1.

Surprisingly, when the 1995 summer outbreak began, it was almost exclusively due to O1 vibrios, and O139 was