DAY 4
ABSTRACT 2

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Pathogenesis of ARIA

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Background: AD is characterised pathologically by the deposition of amyloid-beta peptides in the extracellular spaces of the brain as plaques and cerebral amyloid angiopathy (CAA). Observations on human post-mortem brains and experimental studies in mice demonstrate that amyloid-beta is deposited in the basement membranes of capillaries and basement membranes of arterial smooth muscle cells, within the Intramural Periarterial Drainage (IPAD) pathways.

Method: Pathological studies performed on human post-mortem brains from the first ELAN trial demonstrated that after active immunization against amyloid-beta, despite the disappearance of plaques, CAA worsened and both Abeta 40 as well as Abeta42 were present in the vascular wall. This suggests that Abeta42 solubilised from plaques has become entrapped in the IPAD pathways.

Result: Experimental immunization in rodents against a cerebral protein demonstrate that within 24h, immune complexes are formed in the basement membranes of capillaries, impairing IPAD. By 7 days after immunization, inflammatory cuffs of perivascular cells are present, but, in a normal adult mouse, IPAD is restored.

Conclusion: This suggests that clearance of fluid and solutes can be restored even in the context of immune cell recruitment if the vascular wall is healthy.