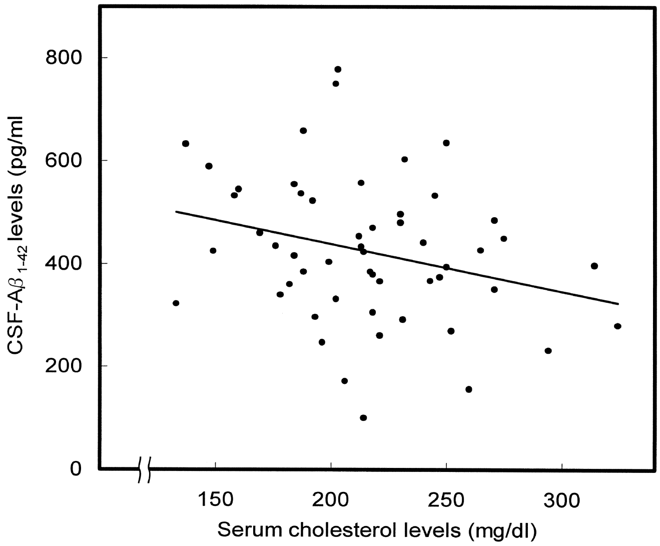

Figure 1. A simple correlation between serum cholesterol levels and cerebrospinal fluid (CSF) levels of amyloid-β (Aβ) protein ending at amino acid 42 position (CSF-Aβ_{1-42}) in Alzheimer's disease.

gression of dementia.[5] Therefore, the low levels of CSF-Aβ_{1-42} in AD are likely to reflect progressive accumulation of Aβ in the brain tissue.[5] Our previous study also demonstrated that CSF-Aβ_{1-42} levels in AD patients significantly correlated with cerebral glucose metabolism.[6] These results suggest that the CSF-Aβ_{1-42} levels may reflect residual brain function in AD patients. Therefore, our findings suggest that reduction in the serum cholesterol levels by lipid-lowering agents such as statins may lead to an increase in the CSF-Aβ_{1-42} levels, which might reflect rescue of brain neurons from Aβ-induced neurotoxicity. Further clinical trials of statins aiming at decreasing the risk of developing AD or delaying the progression of AD need to be conducted in a prospective manner.

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FOLATE DEFICIENCY AND RISK OF PNEUMONIA IN OLDER PEOPLE

To the Editor: Swallowing disorders are common in older people and lead to substantial morbidity and mortality due to aspiration pneumonia.[1] Delayed triggering of the swallowing reflex occurs frequently in patients with infarctions in the basal ganglia; these patients are susceptible to the development of aspiration pneumonia.[2] Dopamine, a neurotransmitter in the brain, plays a pivotal role in the regulation of the swallowing function; an impairment of its metabolism is observed in patients with aspiration pneumonia.[3] Folate deficiency is also common in older people, especially in institutionalized subjects.[4] Because folate deficiency causes impaired dopamine metabolism in the central nervous system and might modify brain function,[5–7] we investigated whether aspiration pneumonia is associated with a reduction in plasma folate levels in older patients and whether vitamin supplementation lowers the incidence of pneumonia in such patients.

Institutionalized patients who had had at least two episodes of aspiration pneumonia with chest radiographic evidence of inflammation in the lower pulmonary segments during the preceding 2 years but were not bedridden were eligible. We excluded patients if they had a history of stroke or neurodegenerative diseases or they were immunocompromised, such as those with malignant disease, renal failure, or human immunodeficiency virus-1 infection. Fifteen patients (mean age ± standard error (SE) 71 ± 2) were recruited from nursing homes or other institutions. Magnetic resonance imaging (MRI) of the brain revealed various degrees of atrophy without evident infarctions in all patients. The 12 age-matched controls (mean age ± SE 72 ± 2) were healthy volunteers and had normal MRI findings. None of the participants used vitamin supplementation and all were free from pneumonia for at least 2 months before the study.

We measured fasting plasma concentrations of folate; homocysteine, a sensitive marker of a shortage of cellular folate; vitamin B_{12}; and vitamin B_6, as described previously,[8] at study entry and after folic acid supplementation (5-mg tablet, twice daily) for 8 weeks. The swallowing function was also evaluated by the latency of swallowing reflex[2] at the same intervals. For a prospective study on the incidence of pneumonia, all patients underwent a physical examination and chest radiography. Criteria for diagnosis of pneumonia were a new pulmonary infiltrate seen on a chest radiograph and one of these features: cough, temperature higher than 37.8°C, or subjective dyspnea. The prevalence of pneumonia was examined during folic acid supplementation (5-mg tablet, twice daily) for 2 years. Informed consent was obtained from each subject. Results are reported as mean ± SE. Statistical analysis was performed by one-way analysis of variance and followed by the Newman-Keuls test. Significance was accepted at $P < .05$.

Folate deficiency was found in 13 of 15 patients with aspiration pneumonia (Table 1), whereas none of the controls had folate deficiency. Two patients with normal plasma folate levels were excluded from the subsequent analysis. In 13 patients with aspiration pneumonia, initial plasma homocysteine concentrations were significantly higher (mean 18.2 ± 1.3 μmol/L in patients vs 6.4 ± 0.7 μmol/L in controls, $P = .012$) in association with a significant decrease in plasma folate concentrations (2.4 ± 0.1 ng/mL in patients vs 8.3 ± 0.8 ng/mL in controls, $P = .024$), and the latency of swallowing reflex was significantly prolonged (6.0 ± 0.4 sec in patients vs 1.8 ± 0.1 sec in controls, $P = .008$). No other neurological abnormalities were identified in these patients. There were no significant differences between patients and controls in plasma concentrations of vitamin B_{12} (mean 485 ± 22 pg/mL vs 512 ± 46 pg/mL, respectively, $P = .32$) and VB_6 (52.1 ± 5.2 nmol/L vs 54.8 ± 3.9 nmol/L, $P = .26$). After folic acid supplementation, plasma concentrations of homocysteine and folate were normalized, and the latency of swallowing reflex was significantly improved in patients with pneumonia (1.7 ± 0.1 sec, $P < .001$ compared with pretreatment data) (Table 1). There was no documentation of pneumonia during a 2-year observation period either in controls or in patients with recurrent pneumonia.

The present study demonstrated that the plasma folate concentration was reduced and the plasma homocysteine concentration was increased in older patients with aspiration pneumonia. Folate deficiency may, therefore, be an independent marker for increased risk of aspiration pneumonia in older people. The commonest causes of folate deficiency are either dietary deficiency or malabsorption, both of which are especially common in alcoholics and institutionalized older people.[4] Folic acid supplementation may prevent the incidence of pneumonia, probably by improving the swallowing function in these susceptible subjects. Our results might provide a novel therapeutic strategy for preventing pneumonia in older people.

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Table 1. Fasting Plasma Folate and Homocysteine Concentrations, Latency of Swallowing Reflex* and Frequency of Pneumonia at Baseline and After Folic Acid Treatment in Patients with Aspiration Pneumonia

			Folate Concentrations (ng/mL)		Homocysteine Concentrations (μmol/L)		Latency of Swallowing Reflex (sec)		Frequency of Pneumonia (times)	
Case	Sex	Age	Baseline	After treatment	Baseline	After treatment	Baseline	After treatment	Baseline	After treatment
1	F	66	2.1	9.4	13.2	8.7	5.3	1.7	2	0
2	M	71	2.5	12.0	11.5	6.5	8.4	2.2	3	0
3	M	72	2.6	15.2	11.9	7.0	4.3	1.5	3	0
4	F	67	2.5	9.6	24.0	9.4	9.0	2.4	4	0
5	M	76	2.2	15.6	11.6	8.5	5.7	1.9	2	0
6	M	72	3.3	14.6	21.6	8.3	6.5	1.8	3	0
7	M	69	2.5	18.2	11.9	8.3	5.2	1.5	3	0
8	F	70	2.7	10.1	12.9	4.8	7.2	2.2	3	0
9	F	73	2.2	12.2	17.0	7.6	5.6	1.4	2	0
10	M	67	2.4	18.9	14.6	7.4	4.8	1.2	2	0
11	M	74	2.1	19.2	12.6	8.2	4.2	1.4	2	0
12	M	75	2.2	14.7	17.2	8.0	7.4	1.5	4	0
13	F	71	2.1	13.8	13.9	7.6	4.9	1.8	2	0

*The swallowing reflex was induced by a bolus injection of 1 mL distilled water into the pharynx through a nasal catheter. The latency of swallowing reflex was evaluated as the time from the injection to the onset of swallowing.[2]
F = female; M = male.