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Variant of TREM2 associated with risk of Alzheimer's disease

Alzheimer's disease is the most common form of dementia in the elderly. The disease is characterized by the formation of extracellular amyloid plaques, intracellular neurofibrillary tangles, and loss of neurons, which results in brain atrophy and progressive loss of cognitive function. Variants in the genomic sequence, including *APP, PSEN1,* and *PSEN2,* have been described and are associated with the development of Alzheimer's disease prior to 60 years of age. However, the majority of Alzheimer's disease is late onset, and the most common variant associated with this is apolipoprotein E (ApoE). The authors conducted a study to search for additional sequence variants associated with Alzheimer's disease in a patient cohort from Iceland. They performed whole-genome sequencing of samples from 2,261 Icelanders and found 191,777 functional variants, including frameshift, splicing, and stop gain-loss variants. The authors noted that these were the variants most likely to affect protein function. They then imputed these sequence variants into the genomes of patients with Alzheimer's disease and control participants and searched for an association with Alzheimer's disease. They also performed replication tests using case-control series from the United States, Norway, Netherlands, and Germany. The authors concluded that they found a rare missense mutation (rs75932628-T) in the gene encoding the triggering receptor on myeloid cells 2 *(TREM2),* which was found to be a significant risk predictor for Alzheimer's disease in Iceland (odds ratio, 2.92; 95 percent confidence interval, 2.09–4.09). Interestingly, the study also showed that carriers of the mutation rs75932628-T who were between the ages of 80 and 100 years and who did not have Alzheimer's disease had poorer cognitive function than noncarriers. The authors hypothesized that the variant *TREM2* may impair the inflammatory process, leading to an increased predisposition to Alz-heimer's disease.

Jonsson T, Stefansson H, Steinberg S, et al. Variant of *TREM2* associated with the risk of Alzheimer's disease. *N Engl J Med.* 2012. doi:10.1056/NEJMoa1211103.

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Policy statement on Clostridium difficile infection in infants and children

Clostridium difficile is the most common cause of antimicrobial-associated diarrhea and infection in hospitalized children, and its incidence is increasing. *C. difficile* is a spore-forming, anaerobic, gram-positive bacillus that produces toxins A and B, which are responsible for the intestinal disease associated with infection. The emergence of an epidemic strain of toxin-producing *C. difficile*, NAP1, may be the cause of the increased number of infections in children. Recent guidelines developed for adult *C. difficile* infections (CDIs) do not address pediatric-specific issues. The American Academy of Pediatrics recently published a policy statement for CDIs in infants and children. The purpose of the policy statement is to provide pediatricians with updated information and recommendations about CDIs in pediatric patients. The challenge of determining the rate of CDIs is whether the presence of the microbe represents true disease or asymptomatic carriage. In infants, testing for *C. difficile* is not recommended in a setting where there is a high prevalence of asymptomatic carriage. Testing should be limited to infants with Hirschsprung disease or other severe motility disorders, or to instances of *C. difficile* outbreak. In addition, *C. difficile* toxin cannot be assumed to be the causative agent for diarrhea in children who have not reached adolescence. For example, in two studies of hospital inpatients who were newborn to two years of age, 11 to 59 percent of patients with diarrhea and 24 to 33 percent of controls were colonized with *C. difficile.* Transmission is via the fecal-oral route, and controlling contact with the patient or the patient's contaminated environment is critical. A test of cure after treatment of CDI is not recommended due to the microbe and its toxins and genome

shedding for a long period of time after the resolution of diarrheal symptoms. In conclusion, the American Academy of Pediatrics Committee on Infectious Diseases recommends that alternative etiologies be sought in pediatric patients younger than three years old, even with a positive test result for *C. difficile.* A positive test result after the third year of life indicates probable CDI. Endoscopic or histological test results positive for pseudomembranous colitis would indicate a definite infection. The policy also recommends precautions specific to antimicrobial treatment, decontamination, and patient contact.

American Academy of Pediatrics Committee on Infectious Diseases. Policy statement: *Clostridium difficile* infection in infants and children. *Pediatrics.* 2013;131:196–200.

Online version of article and updated information available at http://pediatrics.aappublications.org/content/131/1/196.full.html