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Triplet Repeat Diseases in Man, Microbes, and Molecules

TO THE EDITOR: Dramatic progress has been made in the past 5 years in our understanding of the etiology of more than nine human genetic neuromuscular and neurodegenerative diseases (1). The clinical observation of anticipation can be ascribed to the expansion of triplet repeat sequences. These characteristics were suggested to be involved also in neuropsychiatric syndromes, including forms of dementia, hereditary ataxia, parkinsonism, bipolar affective disorder, schizophrenia, and autism (2–4). The non-Mendelian trait of anticipation may be due to the slippage of the complementary DNA strands during replication. The establishment of a genetically and biochemically tractable system for elucidating the molecular mechanisms that are responsible for expansion, and thus anticipation, would be a significant advance.

It is of interest that *Escherichia coli* shows several remarkable molecular similarities to humans, including 1) genetic instability (expansions and deletions) of triplet repeat sequences (CTG·CAG, CGG·CCG, or AAG·CTT) (1, 5–8), 2) longer repeats that are more unstable than shorter sequences (1, 5–11), 3) preferential expansion of CTG·CAG (9) (this repeat sequence was found in six of the nine triplet repeat diseases), 4) repeat sequence imperfections (polymorphisms) that stabilize long tracts of triplet repeat sequences (1, 5–11), 5) similar types of imperfections (polymorphisms), such as the poly purinepoly pyrimidine motif in the Friedreich's ataxia AAG repeat sequence [7, 8]), 6) approximately similar lengths of the smallest deletion products (10–20 triplet repeats) (1, 5), and 7) DNA polymerases that pause in long CTG·CAG, CGG·CCG, and AAG·CTT sequences (5, 8), which render them susceptible to mutations.

In summary, I submit that certain features of the molecular processes related to the involvement of triplet repeat sequences in human hereditary diseases may be elucidated effectively in simple cellular systems. Obviously, a number of other developmental and neurological questions can only be solved in higher eucaryotic cells. Thus, some features of the "unstable genes—unstable mind" concept (4) may be tractable in genetically defined systems in mice, microbes, and molecules.

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Debating Dissociative Diagnoses

TO THE EDITOR: The diagnosis of dissociative identity disorder, formerly multiple personality disorder, has generated considerable debate. Some argue that the disorder is common and underdiagnosed (1), while others claim that dissociative identity disorder is a rare or frankly artifactual diagnosis (2). Our impression is that dissociative identity disorder is frequently accepted as a valid diagnostic entity in the United States but regarded with greater skepticism in other English-speaking countries.

To test this impression, we collected all articles and letters regarding dissociative identity disorder that appeared between 1976 and 1995 in *The American Journal of Psychiatry*, *The British Journal of Psychiatry*, *The Canadian Journal of Psychiatry*, and *The Australian and New Zealand Journal of Psychiatry*. We rated each article or letter as "skeptical" if it argued that dissociative identity disorder was 1) vastly overdiagnosed or 2) an artifact promoted by suggestive influences. We considered all other articles "nonskeptical," including those that merely acknowledged the existence of literature that was skeptical of dissociative identity disorder. In *The American Journal of Psychiatry*, we found 37 articles and letters, of which five (14%) were rated as skeptical and 32 (86%) nonskeptical. By contrast, in the combined journals from Great Britain and its largest English-speaking commonwealth countries, we found 45 articles and letters, of which 24 (53%) were skeptical, and only 21 (47%) were nonskeptical. This difference in rates of skeptical papers is highly unlikely to be due to chance ($p=0.0003$, Fisher's exact test, two-tailed).

We next examined circulation figures. In the United States, combined individual and institutional subscriptions to *The American Journal of Psychiatry* (46,457) dwarf those of the