

and asks "How often do you attend church, synagogue, or other religious meetings?" Responses are rated as follows: 1=never, 2=once a year or less, 3=a few times a year, 4=a few times a month, 5=once a week, and 6=more than once a week.

The second item is a measure of the nonorganizational dimension and asks "How often do you spend time in private religious activities, such as prayer, meditation or Bible study?" Responses range from 1 (rarely or never) to 6 (more than once a day).

Items 3–5 are three statements that measure subjective or intrinsic religiosity: "In my life, I experience the presence of the Divine," "My religious beliefs are what really lie behind my whole approach to life," and "I try hard to carry my religion over into all other dealings in life." These statements are rated on a scale from 1 to 5 (1=definitely not true; 5=definitely true).

The first two items were taken from large community and clinical studies conducted in North Carolina. They have been administered to almost 7,000 persons aged 18 to 90, and thus there are normative data on response rates in both clinical and community populations. These measures have been related to physical health, mental health, and social support in opposite ways (the organizational dimension related to better health outcomes; the nonorganizational dimension related to poorer outcomes).

The final three items were extracted from Hoge's 10-item intrinsic religiosity scale (2). The Hoge scale was administered to 458 consecutively admitted medical patients. We used regression analysis to examine the relationship between each item on the scale and depressive symptoms, severity of medical illness, functional status, social support, and speed of recovery from depression. Principal component factor analysis of the 10-item scale revealed two major factors: an intrinsic and an extrinsic factor. Three items from the scale were chosen on the basis of their loading on the intrinsic factor, correlation with the total score, and relationship with health outcomes. The 3-item subscale had a Cronbach's alpha of 0.75; while it was strongly correlated with the original 10-item scale ($r=0.85$), it was only moderately correlated with the organizational ($r=0.40$) and the nonorganizational ($r=0.42$) dimensions. Our resulting index (score range=5–27) captures three dimensions of religiosity that are related in overlapping yet unique ways to social support and different health outcomes.

REFERENCES

1. Larson DB, Pattison EM, Blazer DG, Omran AR, Kaplan BH: Systematic analysis of research on religious variables in four major psychiatric journals, 1978–1982. *Am J Psychiatry* 1986; 143:329–334
2. Hoge DR: A validated intrinsic religious motivation scale. *J Scientific Study of Religion* 1972; 11:369–376

HAROLD KOENIG, M.D.
GEORGE R. PARKERSON, JR., M.D.
KEITH G. MEADOR, M.D., M.P.H.
Durham, N.C.

CO₂ Challenge in Nonclinical Subjects

TO THE EDITOR: We read with great interest the 1-year prospective evaluation of nonclinical subjects with no history of spontaneous panic attacks who underwent the 35% CO₂ challenge (1). We agree on the importance of investi-

gating whether laboratory-induced anxiety will induce or "potentiate" panic disorder. These kinds of studies are particularly relevant to test the safety of the 35% CO₂ challenge in the investigation of the pathogenetic mechanisms of panic disorder and in consideration of its possible use as a laboratory diagnostic procedure.

We contacted 34 nonclinical subjects (13 men and 21 women, mean age=29.1 years [SD=4.1]) who previously had been included in a study that examined 35% CO₂ reactivity in panic patients (2). The original group had consisted of 44 individuals, but we were not able to contact 10 of them. The subjects were observed for a mean of 45.9 months (SD=6.1, range=30–53) after the 35% CO₂ challenge. After written informed consent was obtained, each subject was given the anxiety disorders section of the Diagnostic Interview Schedule.

Among these nonclinical subjects, 30 (88%) had never experienced an unexpected panic attack before the challenge and had no history of panic disorder in their family. Four (12%) had shown a positive response to the 35% CO₂ challenge according to a previously defined threshold (3). For these four subjects, the mean values on the Visual Analogue Scale for Anxiety before and after the challenge were 12.8 (SD=14.9) and 16.2 (SD=13.9), respectively, with a mean percentage change in score of -3 (SD=28.1). One of these subjects experienced three panic attacks (but not panic disorder) over a period of 3 years; the first attack occurred 6 months after the challenge. Two subjects had experienced unexpected panic attacks before the challenge, and both had a positive reaction to the 35% CO₂ challenge. One experienced a single panic attack 15 months after the challenge, while the other reported no panic attacks. Two subjects reported a family history of panic disorder. While one had a positive reaction to the 35% CO₂ challenge, neither reported panic attacks after the challenge. No subjects in our cohort developed panic disorder or any other anxiety disorder.

The inhalation of a 35% CO₂/65% O₂ gas mixture was not able to prime panic disorder in nonclinical subjects over a period of 3–4 years, which confirms and extends the findings of Harrington and colleagues (1). This finding thus supports the safety of the 35% CO₂ challenge, at least when administered to nonclinical subjects. Although our report suggests that the 35% CO₂ challenge might be safe also when administered to high-risk subjects, this observation needs to be confirmed in larger study groups that include members of families with panic disorder patients and subjects with sporadic, unexpected panic attacks, in particular those who show a positive response to the 35% CO₂ challenge (4–6). These studies are currently ongoing at our center.

REFERENCES

1. Harrington PJ, Schmidt NB, Telch MJ: Prospective evaluation of panic potentiation following 35% CO₂ challenge in nonclinical subjects. *Am J Psychiatry* 1996; 153:823–825
2. Perna G, Battaglia M, Garberi A, Arancio C, Bertani A, Bellodi L: CO₂/O₂ challenge test in panic disorder. *Psychiatry Res* 1994; 52:159–171
3. Battaglia M, Perna G: The 35% CO₂ challenge in panic disorder: optimization by receiver operating characteristic (ROC) analysis. *J Psychiatr Res* 1995; 29:111–119
4. Perna G, Cocchi S, Bertani A, Arancio C, Bellodi L: Sensitivity to 35% CO₂ in healthy first-degree relatives of patients with panic disorder. *Am J Psychiatry* 1995; 152:623–625
5. Coryell WH: A trait marker for panic disorder (letter). *Biol Psychiatry* 1996; 39:567
6. Perna G, Gabriele A, Caldirola D, Bellodi L: Hypersensitivity to

inhalation of carbon dioxide and panic attacks. *Psychiatry Res* 1995; 57:267-273

GIAMPAOLO PERNA, M.D., PH.D.
SILVIA COCCHI, M.D.
ERNESTINA POLITI, M.D.
LAURA BELLODI, M.D.
Milan, Italy

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.

REFERENCES

1. Davies K, Warren S (eds): *Genome Analysis*, vol 7: *Genome Rearrangement and Stability*. Cold Spring Harbor, NY, Cold Spring Harbor Laboratory Press, 1993
2. Morris AG, Gaitonde E, McKenna PJ, Mollon JD, Hunt DM: CAG repeat expansions and schizophrenia: association with disease in females and with early age-at-onset. *Hum Mol Genet* 1995; 4:1957-1961
3. Margolis RL, Stine OC, McInnis MG, Ranen NG, Rubinsztein DC, Leggo J, Jones-Brando LV, Kidwal AS, Loev SJ, Breschel TS, Callahan C, Simpson SG, DePaulo JR, McMahon FJ, Jain S, Paykel ES, Walsh C, DeLisi LE, Crow TJ, Torrey EF, Ashworth RG, Macke JP, Nathans J, Ross CA: cDNA cloning of a human homologue of the *Caenorhabditis elegans* cell fate-determining gene *mab-21*: expression, chromosomal localization and analysis of a

highly polymorphic (CAG)_n trinucleotide repeat. *Hum Mol Genet* 1996; 5:607-616

4. Petronis A, Kennedy JL: Unstable genes—unstable mind? *Am J Psychiatry* 1995; 152:164-172
5. Wells RD: Molecular basis of genetic instability of triplet repeats. *J Biol Chem* 1996; 271:2875-2878
6. Kang S, Jaworski A, Ohshima K, Wells RD: Expansion and deletion of CTG repeats from human disease genes are determined by the direction of replication in *E coli*. *Nat Genet* 1995; 10:213-218
7. Campuzano V, Montermini L, Molto MD, Pianese L, Cossee M, Cavalcanti F, Monros E, Rodius F, Duclos F, Monticelli A, Zara F, Canizares J, Koutnikova H, Bidichandani SI, Gellera C, Brice A, Trouillas P, De Michele G, Filla A, De Frutos R, Palau F, Patel PI, Di Donato S, Mandel J-L, Coccozza S, Koenig M, Pandolfo M: Friedreich's ataxia: autosomal recessive disease caused by an intronic GAA triplet repeat expansion. *Science* 1996; 271:1423-1427
8. Ohshima K, Kang S, Larson JE, Wells RD: Cloning, characterization, and properties of seven triplet repeat DNA sequences. *J Biol Chem* 1996; 271:16773-16783
9. Ohshima K, Kang S, Wells RD: CTG triplet repeats from human hereditary disease are dominant genetic expansion products in *Escherichia coli*. *J Biol Chem* 1996; 271:1853-1856
10. Shimizu M, Gellibolian R, Oostra BA, Wells RD: Cloning, characterization, and properties of plasmids containing CGG triplet repeats from the FMR-1 gene. *J Mol Biol* 1996; 258:614-626
11. Kang S, Ohshima K, Jaworski A, Wells RD: CTG triplet repeats from the myotonic dystrophy gene are expanded in *Escherichia coli* distal to the replication origin as a single large event. *J Mol Biol* 1996; 258:543-547

ROBERT D. WELLS, PH.D.
Houston, Tex.

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