

Factors In The Panic-Agoraphobia Transition

David A. Katerndahl, M.D.

Abstract: A cause-and-effect relation between panic attacks and agoraphobia is an accepted concept. It is believed that, left unchecked, a subgroup of patients with panic attacks will consistently develop agoraphobia. However, to date, there are no means for early identification of this at-risk group. This study analyzed patients with panic attacks and phobic avoidance behaviors by using population-based, survey-collected data. Path analysis was used to determine relations among panic symptoms, phobic behaviors, panic-phobic lag times, and measures of pervasiveness and severity of fears and panic. Panic-related chest pain, dyspnea, trembling, and fear were important factors in the develop-

ment, pervasiveness, and severity of situational fears and anticipatory anxiety. However, full-blown agoraphobia was only related to the presence of anticipatory anxiety and the pervasiveness of phobic avoidance behaviors. Although the age-of-onset of panic and phobic avoidance was unrelated to other factors, lag times were dependent upon panic symptomatology and the presence of depression. These findings suggest that patients with panic attacks who are at risk for agoraphobia can be identified by the nature of their panic symptoms, and perhaps, through early treatment, the development of phobic avoidance can be averted. (J Am Bd Fam Pract 1989; 2:10-6.)

There is general acceptance of a cause-and-effect relation between panic attacks and agoraphobia. In the model proposed by Klein,¹ initial spontaneous panic attacks were linked in the patient's mind to the settings in which they occurred. There was anxiety when the patient anticipated being in those settings. This anticipatory anxiety led to avoidant and dependent behaviors until the patient became truly agoraphobic. This relation was supported by genetic studies of agoraphobia and panic disorder;^{2,3} however, these studies emphasized the fact that only a subgroup of panic disorder patients were truly at risk for the development of agoraphobia.

In an attempt to delineate those patients with panic attacks who are at risk for the development of phobic avoidance (situational fears, anticipatory anxiety, avoidance behavior, and fear dominating the patient's life), this study was undertaken. It was hypothesized that certain characteristics of the panic attacks as well as demographic features would correlate with agoraphobic fears and behaviors.

From the Department of Family Practice, University of Texas at San Antonio. Address reprint requests to David A. Katerndahl, M.D., Department of Family Practice, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284.

Supported in part by a grant from the Ohio Academy of Family Physicians.

Methods

This study was based on a secondary analysis of survey data collected in Franklin County, Ohio, and previously reported in the family practice literature.⁴ Details of the survey methodology have been reported and will not be restated here. In summary, of 1000 randomly selected households surveyed, 316 persons representing 210 households responded. There was a telephone follow-up of 30 randomly selected households that did not respond. Using chi-square and t-test analyses, no significant differences were found in demographics or the presence of the *Diagnostic and Statistical Manual of Mental Disorders-III* diagnoses of panic disorder, major depressive disorder, or agoraphobia when respondents were compared with those who did not respond. In addition, when all respondents were compared demographically with the 1980 census data for Franklin County, there were no significant differences in age and gender. Therefore, the entire study group was believed to be similar demographically to the population in Franklin County.

The screening instrument was developed through an iterative process to provide maximum validity and reliability. In addition, pilot testing was performed in both panic attack patients and control patients to assess reliability. Subsequent comparison of the screening instrument with the *Diagnostic Interview Schedule*⁵ showed that, in panic attacks, the sensitivity of the screening in-

strument was 84.4 percent and the specificity was 92.3 percent. Phobic avoidance was assessed by the presence of fear in specific situations (driving, going to the supermarket, etc.), the presence of anticipatory anxiety about those fears, and whether the fear dominated the patient's life, the ultimate criterion for a diagnosis of agoraphobia.⁶

Path analysis classically uses standardized regression coefficients generated from multiple regression analysis. This procedure was not used here because of the small sample size ($n = 37$). In this study, path analysis was performed on the data using an initial process of Pearson correlations followed by correction of the initial path using partial correlation assessments. Partial correlations between the dependent variable and all of the statistically significant independent variables were obtained after the effect of the independent variable with the highest correlation was removed. At each step, variables losing statistical significance were eliminated, while the variable with the subsequent highest correlation was retained and adjusted for in the next partial correlation. An alpha level of 0.05 was used. Power analysis indicates that when using 37 panic attack patients and seeking a large effect size defined as a correlation coefficient of 0.5, the power is 95 percent. Similarly, when using the same effect size but a sample size of 33 to reflect those having some agoraphobic fears, the power is 92 percent. Ordinal data were correlated using Spearman's correlation coefficient.

The limitations of this study were primarily those associated with survey research, which relied heavily upon patients' recall of panic attack experiences as well as the uniformity of experi-

Table 2. *Description of Interval Data.*

Variable	Range	Mean	SD
Panic attack severity (number of symptoms)	4-12	4.66	2.98
Pervasiveness of fears (number of fears)	1-7	2.75	1.92
Pervasiveness of anticipatory anxiety (number of fears)	1-5	2.19	1.52
Age at first panic attack (years)	15-70	36.54	16.04
Age at onset of fears (years)	4-75	33.48	18.31
Age at onset of anticipatory anxiety (years)	4-74	36.19	19.80
Panic-fears lag time (years)	0-13	3.18	4.49
Fears-anticipatory anxiety lag time (years)	0-10	0.58	2.06
Panic-anticipatory anxiety lag time (years)	0-13	3.80	4.57

ences. Concurrent validity was assessed using the panic attack portion of the survey instrument, but the depression and agoraphobia sections were not evaluated. Although every effort was made to follow up on households that did not respond, the low response rate may alter some of the findings. However, this study focuses on the patients identified with panic attacks and agoraphobia and is not used to fix prevalence rates. Therefore, with the high specificity of this instrument, the conclusions of this study should be valid.

Results

The study sample consisted of 24 patients with panic disorder, 10 with panic disorder and mild-to-moderate phobic avoidance, 3 with agoraphobia with panic attacks, 16 with some phobic avoidance but without full-blown panic attacks, and 4 with agoraphobia without panic attacks. Approximately 70 percent of the panic attack patients and 100 percent of the agoraphobic patients were women. Both groups were similar in terms of age distribution; half were ≤ 35 years old. Ordinal and interval variables are described in Tables 1 and 2, respectively.

Several variables used in this analysis had a judgment quality to them. The number of symptoms during a panic attack was used to estimate panic severity. Similarly, the number of times a patient left home during the week was used to assess the severity of phobic avoidance. On the other hand, the pervasiveness of the phobic fears

Table 1. *Description of Ordinal Data.*

Variable	Descriptor	Frequency n (percent)
Frequency of panic attacks	≥ 1 per day	2 (5.4)
	> 2 per week	9 (24.3)
	1 per week	6 (16.2)
	1-2 per month	11 (29.7)
	< 1 per month	9 (24.3)
		37
Number of times leaving home	≤ 3 per week	6 (21.4)
	4-7 per week	6 (21.4)
	7-10 per week	3 (10.7)
	10-15 per week	1 (3.6)
	> 15 per week	12 (42.9)
		28

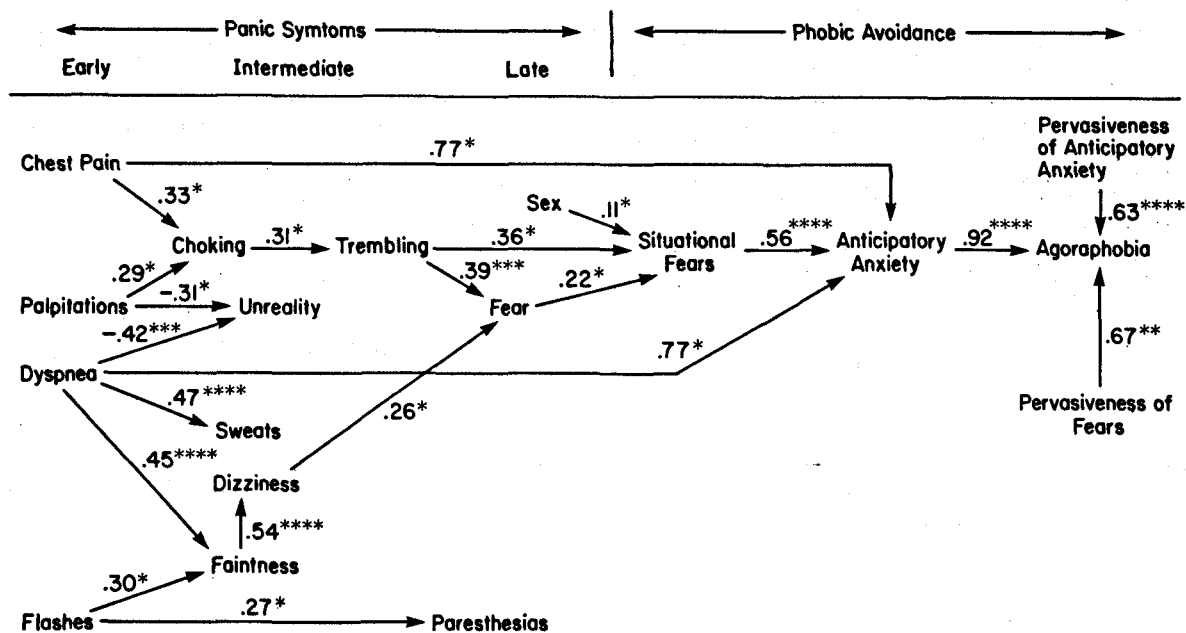


Figure 1. Interrelations of panic symptoms and phobic behavior. The numbers shown represent partial correlation coefficients.

* = $P \leq 0.05$; ** = $P \leq 0.01$; *** = $P \leq 0.005$; **** = $P \leq 0.001$.

and the anticipatory anxiety were measured by the number of situations in which fear occurred and anticipatory anxiety experienced, respectively.

Figure 1 shows the results of path analysis on the interrelations of panic symptoms and phobic avoidance. The temporal ordering of panic symptoms was based upon previous panic sequence work.⁷ The ordering of phobic avoidance variables was based on theoretical constructs. What was specifically significant was that the initial step in the phobic avoidance sequence was the presence of fears in a variety of situations. Specific factors related to this were presence of trembling during panic attacks as well as fear of dying, going crazy, or losing control. Female gender was also a relevant factor in this sequence. Presence of anticipatory anxiety was strongly related to the onset of the phobic fears already mentioned, but it was also heavily influenced by the presence of dyspnea and chest pain during panic attacks. However, full-blown agoraphobia, in which these fears and behaviors dominate the patient's life, was not related to the initial fears or panic-related symptomatology. Instead, it was dependent upon the presence of anticipatory anxiety and, to a great degree, the pervasiveness of both the fears and the anticipatory anxiety.

Figure 2 shows the relations of phobic severity and pervasiveness. Although all three measures of

pervasiveness and severity were interrelated, important demographic and panic symptom variables also have been noted. Again, the presence or absence of chest pain appeared to be a significant variable in the equation.

The final path analysis examined the interrelations of onset of panic and avoidance behaviors. Using partial correlations, all other extraneous variables were eliminated, and the age of the patient and the onset of panic, fears, and anticipatory anxiety were the four key interrelated variables in this path (Figure 3).

However, the lag time between the onset of panic and the onset of fears was strongly related to the presence of depression ($r = -0.83$, $P < 0.01$). This lag time, in turn, was strongly related to the overall lag time between panic attacks and the onset of anticipatory anxiety ($r = 0.99$, $P < 0.001$). However, the lag time between the onset of fears and the onset of anticipatory anxiety was not significantly correlated with either of the other two lag times. Shortened lag time between fears and anticipatory anxiety was associated with the presence of palpitations, dizziness, and trembling during the panic attacks as well as the overall severity of these attacks. Indeed, this last lag time was generally very short; only 1 of the 28 patients with phobic fears did not have anticipatory anxiety. This extremely short lag time may

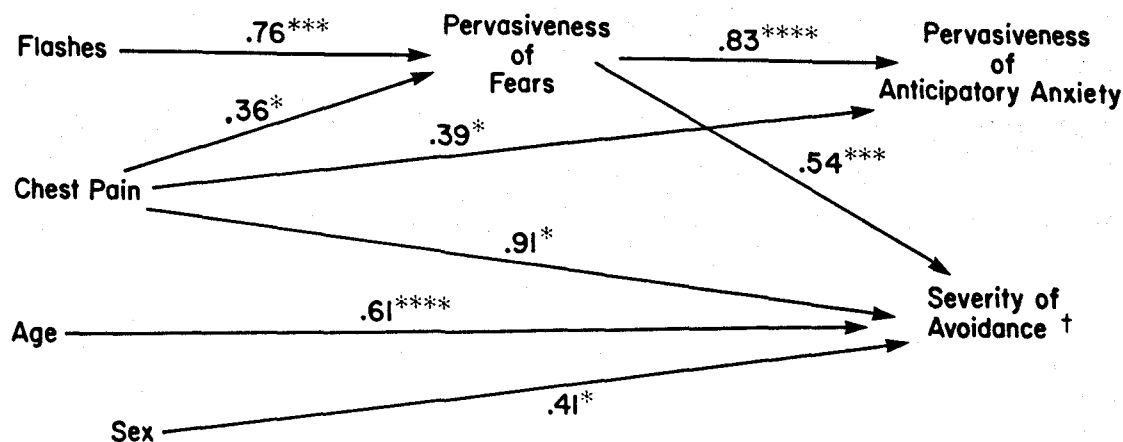


Figure 2. Correlates of phobic severity and pervasiveness.

†Correlation coefficients related to severity of avoidance have been multiplied by (-1) to reflect consistent directionality.

* = $P \leq 0.05$; ** = $P \leq 0.01$; *** = $P \leq 0.005$; **** = $P \leq 0.001$.

have accounted for the lack of significant correlations with other variables.

There were significant differences in the pervasiveness and severity of the agoraphobia, depending upon whether the fears dominated the patient's life. Those with full-blown agoraphobia had significantly more pervasive fears ($t = 4.46$, $P < 0.001$) and more pervasive anticipatory anxiety ($t = 7.41$, $P < 0.001$). Differences in severity and pervasiveness of agoraphobia as well as the frequency and severity of panic attacks were not found in the presence of phobic fears, anticipatory anxiety, or panic attacks.

Discussion

Because a cause-and-effect relation between panic attacks and agoraphobia is supported from a number of research avenues, not only is agoraphobia rarely found in the absence of preceding panic attacks,^{8,9} but demographic, psychometric, and clinical features of the two groups differ little.¹⁰ This relation is further supported by the covariation of panic and agoraphobic fear¹¹ as well as path analysis of treatment studies.¹² Figure 1 shows the interrelations of the panic-associated symptoms. The grouping of symptoms found in this study is in substantial agreement with those found by Cameron, et al.¹³ Four of the panic-associated symptoms appear to be related to the onset of situational fears and anticipatory anxiety—fear of dying, losing control, or going crazy; trembling; chest discomfort; and dyspnea. Although previous work has suggested that the severity of these

symptoms in most panic sufferers is not unusually high, the severity of trembling is second only to that of palpitations.¹⁴ When severity of the symptoms, however, has been compared in panic disorder and agoraphobic patients, individual symptom severity does not seem to be greater for any symptoms in the agoraphobia patients.^{11,13} It appears, therefore, that the presence of these symptoms is the key factor rather than their severity.

Specific panic-related symptoms have been linked to fearful cognitions.¹⁵ The fear component of panic attacks, in particular, may represent a learned response to the somatic symptoms.^{7,16} For example, lactate infusion producing panic attacks in susceptible persons may result in panic attacks without the presence of the fear component.¹⁷ By the same token, the fear present during panic attacks appears to be different from other naturally occurring fear responses.^{18,19}

Hence, the presence of specific panic-related symptoms is associated with phobic avoidance events. Patients having panic attacks with chest pain, trembling, dyspnea, and fear may be at greater risk for the development of agoraphobia. Control of these symptoms may alleviate some of this risk. This concept is supported by the work of Franklin²⁰ in which the initial fears were the fear of panic, losing control, dying, and going crazy. But over time, as the agoraphobia progressed, the situational fears rose dramatically, while the panic-related fears and somatic fears declined.

The medical literature has suggested that there are premorbid features in those who develop agoraphobia including such variables as family

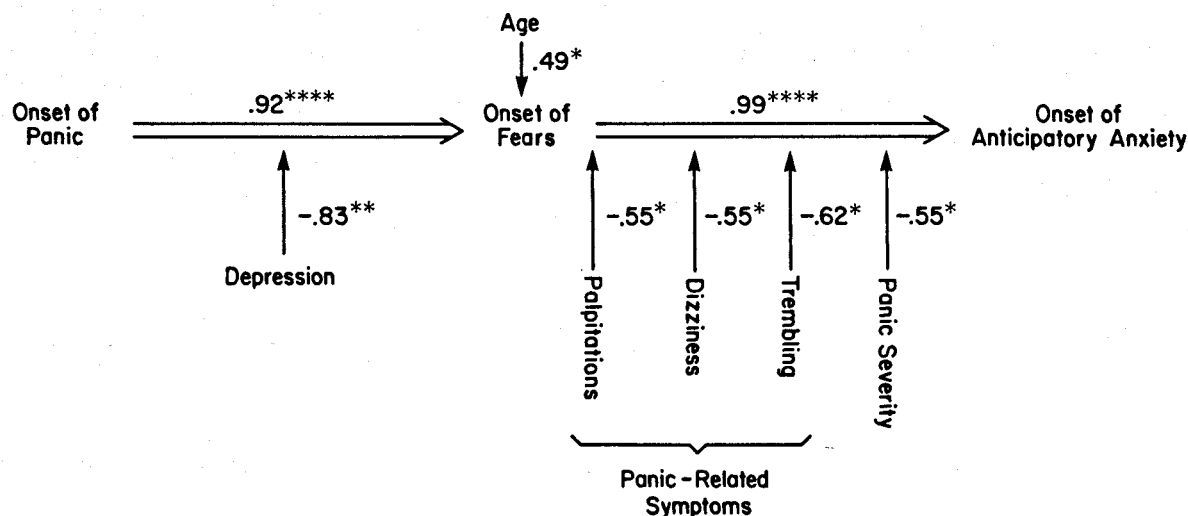


Figure 3. Correlates with ages of onset and lag times.

→ = Factors; ⇒ = Lag times; * = $P \leq 0.05$; ** = $P \leq 0.01$; *** = $P \leq 0.005$; **** = $P \leq 0.001$.

history, life development, trait anxiety, introversion, narcissism, and emotional dependence.²¹ Although these findings have not been universally supported,²² recent work has suggested that agoraphobics have a high degree of interpersonal sensitivity and paranoid ideation²³ as well as dependent personality characteristics.²⁴ However, dependent traits tend to improve with treatment, suggesting that they may be a manifestation of the disorder and not a risk factor, whereas other personality traits such as avoidant and histrionic characteristics do not improve with therapy.²⁵

Although child separation anxiety is increased in both panic disorder and agoraphobia, the difference is especially pronounced in the agoraphobic group²⁶ and, indeed, includes other childhood psychiatric disorders as well.²³ In addition, other risk factors for the development of agoraphobia include female gender, presence of depression, and the number and severity of panic attacks.^{23,27,28} Finally, coping behavior may also play a role in the development of agoraphobia. Patients with panic disorder who use problem-focused coping mechanisms have lower levels of depression and anxiety, while those using wishful thinking show the opposite pattern. Similarly, wishful thinking predisposes the patient to a greater number of phobias, while those seeking social support appear to protect themselves from the development of phobias.²⁹

Although this study does not focus on personality characteristics or coping behaviors, there are similarities between its results and that of the

literature. Female gender is associated with the development of situational fears, and characteristics of panic attacks are relevant not only to situational fears but also to the development of anticipatory anxiety. However, the number and frequency of panic attacks are not correlated with any measures of phobic avoidance. Instead, the pervasiveness of the situational fears and anticipatory anxiety are key factors in the development of full-blown agoraphobia.

As Figure 2 indicates, the pervasiveness and severity measures of agoraphobia are interrelated. The degree to which the patient is housebound is related to the age of the patient as well as to being female. A critical factor in the entire scheme is the presence of chest pain during panic attacks. Not only is chest pain important in the development of anticipatory anxiety, but it is relevant to the pervasiveness of situational fears and anticipatory anxiety, in addition to the severity of the avoidance. The importance of chest pain in panic attacks is supported by studies indicating a high frequency of panic disorder in patients having normal coronary angiography and chest pain^{30,31} as well as in those presenting to an emergency room with chest pain.³²

This study indicates that, although the patient's age and the age of onset of panic attacks, situational fears, and anticipatory anxiety are all highly interrelated, there are no extraneous factors important to any ages of onset. Consequently, there appear to be no important variables affecting when the onset of panic attacks or agoraphobia occurs.

On the other hand, the lag times between attacks, situational fears, and anticipatory anxiety do appear to be related to a few key factors. Previous work has suggested that the time between the onset of panic attacks and the development of agoraphobia is related to the patient's cognitive assessment of the attack and its spontaneity.³³ In this study, the only relevant factor in the lag time between the onset of panic attacks and situational fears is the presence of depression. This link is of particular concern in view of the frequent association of panic and depression in adolescents.³⁴ The lag time between situational fears and the onset of anticipatory anxiety, on the other hand, is directly related to the panic attacks themselves. The severity of panic attacks as well as the presence of trembling, dizziness, and palpitations during panic attacks is associated with a more rapid onset of anticipatory anxiety.

In conclusion, this study indicates that the characteristics of the panic attacks are important factors in the development of phobic avoidance and in its pervasiveness and severity. Whereas trembling and fear are key elements in the development of situational fears, the presence of chest pain is important to all measures of pervasiveness and severity in addition to the onset of anticipatory anxiety. The presence of dyspnea, hot and cold flashes, and trembling is related to the onset of anticipatory anxiety, pervasiveness of such fears, and the rapidity with which anticipatory anxiety develops. However, severity of the panic attacks is related only to the rapidity with which anticipatory anxiety develops.

Conclusion

Because of their practice of comprehensive care, home visits, and close doctor-patient relations, family physicians are in an ideal position for early recognition of panic and agoraphobia. Based upon this study, it is possible to identify patients with panic attacks who are at significant risk for the development of phobic avoidance; namely, females with panic attacks including trembling, fear of dying, going crazy, or losing control. Once the initial situational fears have begun, it may be possible to identify those who will develop the full-blown agoraphobic syndrome—those with chest pain, dyspnea, or both during attacks. This study also suggests not only who will have more severe and pervasive disease but also the rapidity with which phobic avoidance will progress. Perhaps

through this identification of those at risk, early treatment and suppression of panic attacks can circumvent the development of agoraphobia.

I wish to thank Ms. Imelda Garza for her technical assistance with this manuscript.

References

1. Klein DF. Anxiety reconceptualized. In: Klein DF, Rabkin JG, eds. *Anxiety: new research and changing concepts*. New York: Raven Press, 1981: 235-65.
2. Torgerson S. Genetic factors in anxiety disorders. *Arch Gen Psychiatry* 1983; 40:1085-9.
3. Noyes R Jr, Crowe RR, Harris EL, Hamra BJ, McChesney CM, Chaudhry DR. Relationship between panic disorder and agoraphobia. *Arch Gen Psychiatry* 1986; 43:227-32.
4. Katerndahl DA, Gabel LL, Monk JS. Comparative symptomatology of phobic and nonphobic panic attacks. *Fam Pract Res J* 1986; 6:106-13.
5. Robins LN, Helzer JE, Croughan J, Ratcliff, KS. National Institute of Mental Health Diagnostic Interview Schedule. Its history, characteristics, and validity. *Arch Gen Psychiatry* 1981; 38:381-9.
6. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 3rd ed. Washington, D.C.: American Psychiatric Association, 1980.
7. Katerndahl D. The sequence of panic symptoms. *J Fam Pract* 1988; 26:49-52.
8. Weissman MM, Leaf PJ, Holzer CE 3rd, Merikangas KR. The epidemiology of anxiety disorders: a highlight of recent evidence. *Psychopharmacol Bull* 1985; 21:538-41.
9. Garvey MJ, Tuason VB. The relationship of panic disorder to agoraphobia. *Compr Psychiatry* 1984; 25:529-31.
10. Thyer BA, Himle J, Curtis GC, Cameron OG, Nesse RM. A comparison of panic disorder and agoraphobia with panic attacks. *Compr Psychiatry* 1985; 26:208-14.
11. Turner SM, Williams SL, Beidel DC, Mezzich JE. Panic disorder and agoraphobia with panic attacks: covariation along the dimensions of panic and agoraphobic fear. *J Abn Psychol* 1986; 95: 384-8.
12. Klein DF, Ross DC, Cohen P. Panic and avoidance in agoraphobia. Application of path analysis to treatment studies. *Arch Gen Psychiatry* 1987; 44:377-85.
13. Cameron OG, Thyer BA, Nesse RM, Curtis GC. Symptom profiles of patients with DSM-III anxiety disorders. *Am J Psychiatry* 1986; 143:1132-7.
14. Norton GR, Dorward J, Cox BJ. Factors associated with panic attacks in nonclinical subjects. *Behav Ther* 1986; 17:239-52.
15. Rachman S, Levitt K, Lopatka C. Panic: the links between cognitions and bodily symptoms—I. *Behav Res Ther* 1987; 25:411-23.
16. Rapee R, Mattick R, Murrell E. Cognitive mediation in the affective component of spontaneous

- panic attacks. *J Behav Ther Exp Psychiatry* 1986; 119:245-253.
17. Kelly D, Mitchell-Heggs N, Sherman D. Anxiety and the effects of sodium lactate assessed clinically and physiologically. *Br J Psychiatry* 1971; 119:129-41.
 18. Nesse RM, Cameron OG, Curtis GC, Lee M. How antipanic drugs might work. *Am J Psychiatry* 1986; 143:945.
 19. Levin AP, Doran AR, Liebowitz MR, et al. Pituitary adrenocortical unresponsiveness in lactate induced panic. *Psychiatry Res* 1987; 21:23-32.
 20. Franklin JA. The changing nature of agoraphobic fears. *Br J Clin Psychol* 1987; 26:127-33.
 21. Roth M. Agoraphobia, panic disorder and generalized anxiety disorder: some implications of recent advances. *Psychiatr Dev* 1984; 2:31-52.
 22. Tearnan BH, Telch MJ, Keefe P. Etiology and onset of agoraphobia: a critical review. *Compr Psychiatry* 1984; 25:51-62.
 23. Aronson TA, Logue CM. On the longitudinal course of panic disorder: development history and predictors of phobic complications. *Compr Psychiatry* 1987; 28:344-55.
 24. Reich J, Noyes R Jr, Troughton E. Dependent personality disorder associated with phobic avoidance in patients with panic disorder. *Am J Psychiatry* 1987; 144:323-6.
 25. Mavissakalian M, Hamann MS. DSM-III personality disorder in agoraphobia. II. *Compr Psychiatry* 1987; 28:356-61.
 26. Deltito JA, Perugi G, Maremmanni I, Mignani V, Cassano GB. The importance of separation anxiety in the differentiation of panic disorder from agoraphobia. *Psychiatr Dev* 1986; 4:227-36.
 27. Buller R, Maier W, Benkert O. Clinical subtypes in panic disorder: their descriptive and prospective validity. *J Affective Disord* 1986; 11:105-14.
 28. Breier A, Charney DS, Heninger GR. Major depression in patients with agoraphobia and panic disorder. *Arch Gen Psychiatry* 1984; 41:1129-35.
 29. Vitaliano PP, Katon W, Russo J, Maiuro RD, Anderson K, Jones M. Coping as an index of illness behavior in panic disorder. *J Nerv Ment Dis* 1987; 175:78-84.
 30. Katon W, Hall ML, Cormier L, Hollifield M, Vitaliano PP, Beitman BD. Chest pain: the relationship of psychiatric illness to coronary arteriography results. *Am J Med* 1988; 84:1-9.
 31. Beitman BD, Basha I, Flaker G. Major depression in cardiology chest pain patients without coronary artery disease and with panic disorder. *J Affective Disord* 1987; 13:51-9.
 32. Hillard JR, Wuslin L, Hissa D, Rouan G, Geier P. Prevalence of panic disorder and depression among patients presenting to an urban emergency room with chest pain. Presented at the Mental Disorders in General Health Care Settings Conference on June 25-26, 1987, Seattle, Washington.
 33. Breier A, Charney DS, Heninger GR. Agoraphobia with panic attacks. Development, diagnostic stability, and course of illness. *Arch Gen Psychiatry* 1986; 43:1029-36.
 34. Alessi NE, Robbins DR, Dilsaver SC. Panic and depressive disorders among psychiatrically hospitalized adolescents. *Psychiatry Res* 1987; 20:275-83.

GLEANINGS FROM A COMMONPLACE BOOK—NJP

"But the finished man is he who in the midst of the crowd keeps with perfect sweetness the independence of solitude."
R.W. Emerson

"Life is now—whatever it offers, little or much, life is now—this day—this hour—and is probably the only experience of the kind one is to have. As the doctor said to the woman who complained that she did not like the night air, 'Madame, during certain hours of the 24, night air is the only air there is'"

C. Flandrau

"Numerous are the academic chairs, but rare are the wise and noble teachers."
A. Einstein

"The university has, in fact, been swamped by the influx of the mob, and its inmates are themselves becoming only an unconsidered fraction of that mob. In other words, the so called 'liberal' policy in university government has not raised mediocrity to the plane of scholarship, but has degraded scholarship to the plane of mediocrity."
H.T. Peck

"Too many Americans are action-oriented—interested only in the 'bottom line.' We are, generally, doers not feelers. We are for profit, not beauty; just as we are for grades, not education."
N.J. Pisacano