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Current Comments®

Why Is the Ancient and Prevalent Disorder Called Agoraphobia a Neglected Research Topic?

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In previous essays, we've covered a number of psychiatric illnesses including autism,[1] schizophrenia,[2] and depression.[3] Depression, we noted, is a particularly disturbing problem because it is so widespread, and so debilitating. Like depression, agoraphobia is an incapacitating illness. Agoraphobia, however, is less known to the general public.

The third edition of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (*DSM III*)[4] defines phobias as "persistent and irrational fears of an object or situation." To date, scientists have identified phobias ranging from acrophobia, fear of high places, to zoophobia, fear of animals. There is even a phobiaphobia, or fear of fear. But according to the *DSM III*, no phobia is as "severe or pervasive" as agoraphobia.[4] (p. 225)

The term agoraphobia is derived from two Greek words: *agora*, meaning marketplace or place of assembly, and *phobos*, meaning terror or flight.[5] Robert Burton, the British scholar and writer, first described agoraphobia's symptoms in his 1621 work, *The Anatomy of Melancholy*.[6] It wasn't until 1871, however, that C. Westphal coined the term to describe several of his patients who experienced severe anxiety when walking through streets or squares.[5] According to historical accounts, recounted by Isaac M. Marks, Maudsley Hospital, London, in his book *Fears and Phobias*,[7] the French mathematician Blaise Pascal suffered from agoraphobia, as did the Italian writer Alessandro Manzoni. Manzoni, in fact, carried a bottle of concentrated vinegar with him whenever he left home so that he could revive himself if he felt faint.

In her review of the symptomatology of agoraphobia, Diane L. Chambless, Department of Psychiatry, American University, Washington, DC, writes that the primary symptom of agoraphobia is a fear of being away from home, or in any public place from which escape is viewed as difficult.[8] To an agoraphobic, escape can be "blocked" by physical constraints such as those imposed by crowds, or by social constraints that call for highly ritualized, regimented behavior. For instance, acting as a bridesmaid or being the "mother of the bride" would make many agoraphobics very anxious.

Agoraphobics need to feel that they can escape from any situation readily, because for many, panic attacks can strike anytime. During a panic attack, agoraphobics feel dizzy, nauseous, weak in the limbs, and short of breath.[8] Throughout these attacks, agoraphobics may worry that their pounding heart or dizziness will cause them irreparable harm. Typical thoughts include, "I am going crazy," or "I am having a heart attack (or stroke)."[9]

Agoraphobics, therefore, often find that home is the only place where they feel safe, since even if an attack strikes there it will go unobserved, sparing them public embarrassment. Consequently, although their symptoms may wax and wane, some agoraphobics are housebound for years, sometimes for their entire lives. Obviously, this prevents them from working or maintaining a normal

social life. Other agoraphobics can leave home, but only if their spouses or other trusted companions accompany them.

J.A. Mullaney and C.J. Trippett, St. Patrick's Hospital, Gosforth, Newcastle upon Tyne, England, now suspect that some alcoholics actually suffer from agoraphobia.[10] In such cases, agoraphobics first turn to alcohol because it relieves the anxiety they feel when venturing outside,[11] according to physician Arthur B. Hardy, a former agoraphobic, who is now director of TERRAP (for *TERR*itorial *AP*prehensiveness), a nonprofit organization which assists agoraphobics. Although they may eventually seek treatment for their alcoholism, their real problem—agoraphobia—will likely remain untreated.

For most agoraphobics, the onset of the illness is sudden. If panic attacks are part of the disorder, the first one usually occurs between ages 18 and 35. Common sites for attacks include supermarkets, elevators, escalators, parties, crowds, tunnels, bridges, airplanes, and theaters.[12] After the attack, the agoraphobic avoids returning to the place where it occurred for fear of triggering another episode. This phobic avoidance then increases to include other places.

In the last few years, a large volume of literature on agoraphobia has appeared in the scientific as well as the popular press. Marks traces the emergence of this interest to a 1965 BBC radio broadcast about agoraphobia.[7] After the broadcast, 300 listeners wrote to the station for further information. The program generated such interest that eventually an organization to help agoraphobics was established—the Open Door Organization. Within a few months, 1,600 people had joined the group.[7] Incidentally, we did a search of *Science Citation Index®* (*SCI®*) and *Social Sciences Citation Index®* (*SSCI®*): Marks's book, *Fears and Phobias*,[7] which reviews the phenomenology and treatment of phobias, including agoraphobia, has been cited over 325 times since its publication in 1969, qualifying it as a *Citation Classic™*.[13]

According to a study by Stewart Agras, Department of Psychiatry, University of Vermont, Burlington, and colleagues, from one to two million people in the US alone suffer from agoraphobia,[14] although the actual number of victims may be much higher. Since agoraphobics are reluctant to leave home, many are never identified. Often ashamed or embarrassed by their symptoms, they may become so adept at avoiding fear-inducing situations that even their spouses may not realize they have the disorder,[15] according to Claire Weekes, Rachel Forster Hospital, Cremorne Point, Australia.

There are several theories regarding the etiology of agoraphobia. One prominent view is supported by Weekes, Chambless, and Alan J. Goldstein, Department of Psychiatry, Temple University Medical School, Philadelphia. They believe that stress precipitates the first panic attack.[16,17] Events which can trigger an attack include the death of a loved one, a miscarriage, or a divorce. Even happy events such as childbirth or marriage can elicit an attack, since they can also promote stress.[9]

For years, the etiology of agoraphobia was described in terms of psychoanalytic theory, as Wallace H. Vale and Sylvester R. Mlott, Department of Psychiatry, Medical University of South Carolina, Charleston, note in their review of agoraphobia.[18] This rests upon the premise that earlier, usually infantile, traumas account for adult neuroses. In his review of psychoanalytic theories, John Bowlby, Tavistock Clinic, London, noted that some adherents of a psychoanalytic viewpoint believed that an agoraphobic's fear of leaving home indicated a need to return to the security provided by one's parents.[19] Freud, on the other hand, believed that agoraphobia, like all phobias, was part of an "anxiety neurosis" and had a sexual origin.[20] However, such psychoanalytic theories lack empirical support.[21]

Many behavioral scientists now use one of several etiological models to explain the onset of the disease. Some view

the onset of the disorder in terms of operant conditioning, whereby behaviors are acquired or eliminated depending on their consequences.[17] Accordingly, behavior that is rewarded or *positively reinforced* will be acquired, whereas behavior that is punished will be eliminated.

In the view of Kathleen A. Brehony, Department of Psychology, Virginia Polytechnic Institute and State University, Blacksburg, behavior theory may help explain why approximately 85 percent of all known agoraphobics are women. She believes that societal conditioning of women serves as a powerful backdrop for the development of agoraphobic behavior.[22] In her classic paper,[23,24] Sandra L. Bem, Department of Psychology, Stanford University, California, asserts that males are reinforced for behavior that is aggressive, independent, and competent. Females, however, are reinforced for submissive, passive, fearful, and nonassertive behavior[23]—behavior that is characteristic of agoraphobics. After reviewing the literature linking agoraphobia with women, Brehony was prompted to ask, " 'Why are not all women agoraphobic?' rather than, 'Why are some women agoraphobic?' "[22]

Male agoraphobics are less likely to be as severely homebound as their female counterparts. This may also be due to societal stereotyping. Traditionally, men are expected to be the breadwinners, which usually requires them to work outside the home. Most male agoraphobics learn to tolerate the trip to and from work, but venturing elsewhere makes them anxious. Weekes calls this the "city-bound executive syndrome."[16]

Other researchers are investigating a possible biochemical basis for agoraphobia. In the mid-1970s, D. Eugene Redmond, Department of Psychiatry, Yale University, New Haven, Connecticut, and colleagues discovered that victims of panic attacks produced an excess of brain norepinephrine and other neurotransmitters.[25] Neurotransmitters are chemical carriers that transport message impulses across nerve synapses. Indeed, certain drugs such as imipramine and phenelzine, which decrease norepinephrine production, also block panic attacks. Although these drugs have complex effects, in their review of the literature, Dennis S. Charney, Yale University School of Medicine, and colleagues report some scientists believe that their antipanic effects may be due to their effect on norepinephrine.[26]

As with other psychiatric illnesses, there may be a genetic basis for agoraphobia. Several studies found a higher incidence of phobias among family members than among the general public. In a study by R.C. Bowen and J. Kohout, Department of Psychiatry, University of Saskatchewan, Saskatoon, Canada, 84 percent of the agoraphobics questioned could identify a close relative who suffered from an emotional disorder.[27] Moreover, a study by Gregory Carey, University of Minnesota, Minneapolis, found that agoraphobia was more prevalent among identical twins than among fraternal twins.[28]

For agoraphobia to be effectively treated it must, of course, be accurately diagnosed. But this can take years. Seventy percent of the agoraphobics participating in a study by David V. Sheehan, Department of Psychiatry, Massachusetts General Hospital, Boston, and colleagues reported seeing ten or more physicians before a correct diagnosis was made.[29]

Typically, agoraphobics first approach their family physician after experiencing one or more panic attacks. Often, physicians focus on the physiological components such as the patient's pounding heart or dizziness.[21] They may then prescribe diazepam (Valium) or another antianxiety agent. In fact, a nationwide survey of agoraphobics by E.H. Uhlenhuth, Department of Psychiatry, University of Chicago, Illinois, and colleagues found that a full 55 percent had used an antianxiety agent.[30] Ninety-eight percent of the patients participating in the Sheehan study said that they had been treated with what were often

very high doses of tranquilizers for up to 15 years.[29] Whether these agents actually reduce panic attacks is still under debate. While the prevailing opinion has been that these agents are ineffective against panic attacks,[31] a recent paper by Russell Noyes and colleagues, Department of Psychiatry, University of Iowa, College of Medicine, Iowa City, reports the results of a study which found that "diazepam reduced the number and severity of panic attacks."[31]

Diagnosed agoraphobics rarely recover from the disorder without professional assistance. And since misdiagnosis is prevalent, the outlook for most patients has been bleak,[32] according to Lars Jansson and Lars-Göran Öst, Psychiatric Research Center, Ulleråker Hospital, Uppsala, Sweden. However, for those who do receive competent professional help, at least partial recovery is likely.

Up until the early 1960s, psychiatrists usually treated agoraphobics with psychotherapy. This is not surprising considering psychotherapy's popularity at the time, and the paucity of other available treatments. Chambless and Goldstein, however, believe that psychotherapy by itself is impotent against agoraphobia.[9] By the way, they are the editors of *Agoraphobia: Multiple Perspectives on Theory and Treatment*,[33] a comprehensive overview of agoraphobia which was used heavily in preparing this essay.

In the mid-1960s, some therapists began treating agoraphobia with systematic desensitization which, as Matig Mavissakalian, Western Psychiatric Institute and Clinic, and University of Pittsburgh School of Medicine, Pennsylvania, and David H. Barlow, Department of Psychology, State University of New York, Albany, note in their review of phobias, was then being used to successfully treat many other phobias.[34] Systematic desensitization involves exposing the phobic to the objects or places feared after relaxation exercises are mastered. The exposure is graduated. In several steps, a snake phobic, for example, would progress from just viewing a picture of a snake, to actually handling one. In their review of agoraphobia, however, Jansson and Öst cite studies indicating that systematic desensitization is not effective in treating agoraphobia,[32] probably because it does not allow the patient to experience anxiety in the phobic situation.[17] Although following systematic desensitization agoraphobics may think they are cured, panic attacks usually recur.

The primary behavioral treatment now used is exposure therapy, of which there are two types: imaginal exposure and exposure *in vivo*. During imaginal exposure, the therapist describes in detail situations that the patient previously stated were fearful. When this is done gradually, following relaxation exercises, the therapy closely approximates systematic densensitization. Imaginal exposure, however, can also be conducted rapidly, in which case the therapist forces the patient to visualize the fearful situation until reported anxiety decreases.[32] Rapid exposure is sometimes called "flooding."

In vivo exposure, on the other hand, involves real-life practice. The agoraphobic actually enters the dreaded situations. As with imaginal exposure, *in vivo* exposure can be conducted either gradually or rapidly.[32]

Exposure methods are not only effective, they work quickly and patients can learn them easily. A homebound person treated by exposure may be able to enter a local shop on the first session, a suburban shopping center during the second, and center city on the third.[35] And, in a study of agoraphobics treated by exposure, Paul M.G. Emmelkamp, Academic Hospital, Department of Clinical Psychology, Groningen, the Netherlands, found that once improvements are made, they last. Relapses are rare. Emmelkamp also found that four years after *in vivo* exposure, patients remained improved.[36]

For financial reasons, therapists often administer exposure therapy to a group

of patients rather than to individuals.[9] Group therapy also gives agoraphobics the chance to meet each other, and thus learn that their affliction is not unique. As with Alcoholics Anonymous, they can share coping methods, and form close friendships which they so desperately need.

Not all agoraphobics can be treated with exposure therapy. *In vivo* therapy, in particular, can be very hard on some patients, especially men. A study by R. Julian Hafner, Flinders Medical Centre, Australia, found that of 18 male patients offered graded exposure *in vivo*, 44 percent refused or dropped out prematurely.[37] Only 12 percent of the women subjects refused or terminated treatment prematurely. The study also found, however, that those men who did follow through with the treatment benefited from it as much as the women.

Overall, 60 to 70 percent of patients who undergo exposure therapy improve.[32,38] It is likely that as a result of a therapeutic regimen based on exposure therapy, a patient will be able to lead a life relatively free of panic attacks. Occasionally, however, he or she will probably still be troubled by some of agoraphobia's symptoms. In fact, residual disability is the norm.[38]

Drug therapy is the other major treatment that clinicians use. The successful use of drugs to treat agoraphobia was first reported in a 1962 paper by Donald F. Klein, US Public Health Service, and Max Fink, Hillside Hospital, Glen Oaks, New York.[39] Between October 1958 and July 1961, Klein and Fink treated 125 agoraphobics with imipramine, a tricyclic antidepressant. They found that the drug effectively eliminated the panic attacks associated with the disorder.[39]

Since that time, Klein, Sheehan, and others have found that two classes of antidepressants are effective against the panic attacks associated with agoraphobia: the tricyclic antidepressants and the monoamine-oxidase (MAO) inhibitors.[40] Imipramine remains the most commonly used tricyclic, and is usually prescribed first. If imipramine should fail, psychiatrists may prescribe phenelzine, the most commonly used MAO inhibitor. According to Robert Pohl, Department of Psychiatry, Wayne State University, Detroit, Michigan, and colleagues, imipramine is usually tried first because it does not place the harsh restrictions on one's diet that phenelzine does.[41] Patients taking MAO inhibitors can experience severe and even lethal high blood pressure if they eat foods containing the amino acid tyramine. Examples of such foods are pickled herring, aged cheese, chicken liver, and certain wines.[42]

Antidepressants do not work immediately. It may take up to six weeks of treatment before their effectiveness is apparent.[41] After attacks are relieved, therapists usually continue treatment for six months. Although at that point the patient may be free of panic attacks, it's likely that eventually they will recur. Renewed treatment, however, will once again halt the attacks.

The existence of *ISI/BIOMED*® research front #82-3495, "Clonidine and imipramine and tricyclic antidepressant clinical psychotherapeutic drugs for treating depression, agoraphobia, and panic attacks," is evidence of the current interest in using drug therapy to treat agoraphobia and other affective disorders. Two core papers are associated with this front: "Treatment of agoraphobia with group exposure in vivo and imipramine,"[43] by Klein, Charlotte M. Zitrin, and Margaret G. Woerner, Long Island Jewish-Hillside Medical Center, Glen Oaks, New York, and "Treatment of endogenous anxiety with phobic, hysterical, and hypochondriacal symptoms,"[29] by Sheehan, James Ballenger, University of Virginia School of Medicine, Charlottesville, and Gary Jacobsen, Westwood Lodge Hospital, Westwood, Massachusetts. To date, over 50 publications have cited one or both of these papers, which were published in 1980 in the same issue of *Archives of General Psychiatry*. The

first paper gives the results of a double-blind study that compared the effectiveness of group exposure *in vivo*, combined with the use of either imipramine or a placebo. The study found that while a majority of patients in both groups showed at least moderate improvement, imipramine-treated patients fared better than placebo-treated patients. In the study reported in the second paper, in addition to a placebo and imipramine group, a third group received the MAO inhibitor phenelzine sulfate. Patients assigned to the imipramine and phenelzine groups improved much more than the patients in the placebo group. In addition, phenelzine-treated patients showed more improvement than the imipramine-treated patients.

Given these results, it's not surprising that Klein and several other researchers enthusiastically recommend the use of antidepressants for agoraphobia. In addition to the studies described here, they cite others that show these drugs often block panic attacks, and that 70 percent of the patients treated improve to some extent.[44]

Although these results are encouraging, there are many critics of drug therapy. Imipramine, for example, can have side effects. Even small doses of the drug can produce insomnia, jitteriness, irritability, and palpitations, and will exacerbate panic attacks in one in five agoraphobics.[45] Although in such cases other drugs can be used,[45] many agoraphobics refuse to use these drugs at all.

Chambless and Goldstein have reported that over 25 percent of their agoraphobic patients refuse to take imipramine "because of hypochondriacal concerns, fears of drug-induced discontrol, or adverse reactions to previous drugs."[9] Moreover, they report that most of the remaining 75 percent of their patients are afraid or otherwise hesitant to use the medication. One patient had a full-blown panic attack on the first two nights when it was time for her to take the medication.

In their review of the literature, Michael J. Telch, Blake H. Tearnan, and C. Barr Taylor, Stanford University School of Medicine, California, found that of those who do go through with drug therapy, 35 to 40 percent drop out.[46] This compares to a drop out rate of about ten percent for drug-free behavioral treatments. Also, the relapse rate following discontinuation of drugs is much higher than for exposure therapy. They found that between 27 and 50 percent of patients who improve after drug therapy relapse after withdrawal.[46]

Current therapeutic regimens often comprise elements of both drug and behavior therapy, which seems to reflect a coming together of the two camps. In fact, S. Rovner for the *Washington Post* described a May 1983 meeting on phobia treatments held in White Plains, New York, as "a veritable love feast between the behaviorists and medical model proponents."[47] Many behaviorists, however, still use drugs only for particularly stubborn cases, or for patients who don't wish to take part in behavior therapy. Goldstein has written that the great majority of his patients "cease having panic attacks without the use of medication."[48] On the other hand, some drug proponents such as Klein and Michael R. Liebowitz, Department of Psychiatry, Columbia University, New York, will only use behavior therapy by itself when patients are no longer experiencing spontaneous panic attacks.[49]

While most psychiatrists treat agoraphobics with either drug or behavioral therapy or a combination of both, some recommend a self-help program of treatment. Such programs have appeal because they greatly reduce the need for a therapist's costly time. One of the best-known proponents of self-help therapy for agoraphobics is Weekes. Between 1966 and 1974, Weekes treated 2,000 agoraphobics through "remote direction."[16] This is basically exposure therapy. But instead of personally accompanying patients when they leave home, Weekes encourages them by telephone to conduct the exposure sessions on their own. Then, throughout the therapy program, patients periodically call in to

report on their progress. Weekes's patients can also receive instruction through her three books,[15,50,51] a record album, cassettes, and a quarterly magazine.[16]

Recently, Arthur E. Holden, Center for Stress and Anxiety Disorders, State University of New York, Albany, and colleagues have criticized self-help strategies for agoraphobia. They found that subjects in a self-help program consisting of *in vivo* therapy did not perform the practice required by the manual given them.[52] They also criticized Weekes's claims that her strategies were effective since she used questionnaires to assess effectiveness and her improvement criteria were not made clear.[52]

Through drug and behavior therapy, therapists can now control the most severe symptoms of the disease. But few scientists currently feel the disorder can be cured. Agoraphobics can be brought to the point where they are "in control," but remnants of the disorder commonly persist.[53]

If scientists are to improve on this success rate, they must find new drugs that do not present imipramine's side effects. One promising drug which is receiving increasing attention in the literature is alprazolam (marketed by Upjohn Company under the trade name Xanax). According to Guy Chouinard, Department of Psychiatry, McGill University, Montreal, Canada, and colleagues, alprazolam seems to be effective against panic attacks.[54] Moreover, alprazolam does not seem to cause the side effects associated with antidepressants although, like other benzodiazepines, it may induce drowsiness.[54]

But therapists may also have to view agoraphobia in a larger context. Previously, most therapists did not consider the effect family members might have. A number of researchers have found that family members can help agoraphobics. But in other cases, the spouse can severely impede progress.

Frank Milton, Kenley Ward Kingston Hospital, Kingston-on-Thames, Surrey, England, and Hafner, then at St. George's Hospital Medical School, London, studied 15 agoraphobics. They found that in nine cases, when symptoms improved, marriages deteriorated.[55] In a study of 25 patients, Chambless and Goldstein found that only those that divorced their spouses remained improved.[9] However, a former agoraphobic, Ruth Mass, Miami, Florida, has formed several self-help groups for agoraphobics. Out of 50 members, only one out of six married patients divorced after treatment.[56]

Table 1: A selected list of organizations that counsel agoraphobics.

Agoraphobia and Anxiety Center
Temple University
3975 Conshohocken Avenue
Philadelphia, PA 19131

Freedom from Fear Foundation
Box 261
Etobicoke, Ontario M9C 4V3
Canada

Jovicin Foundation for Agoraphobic Recovery
6569 Cleomoore Avenue
Canoga Park, CA 91307

P.A.S.S. Group Inc.
1042 East 105th Street
Brooklyn, NY 11236

Phobia Clinic
Long Island Jewish-Hillside Medical Center
76th Avenue and 266 Street
Glen Oaks, NY 11004

Phobia Clinic
White Plains Hospital Medical Center
Davis Avenue at East Post Road
White Plains, NY 10601

Phobia Society of America
6191 Executive Boulevard
Rockville, MD 20852

Phobics Society
4 Cheltenham Road
Chorlton-cum-Hardy
Manchester M21 1QN
UK

TERRAP
T.S.C. Corporation
1010 Doyle Street
Menlo Park, CA 94025

Part of the problem may be that agoraphobics often choose mates that they know will care for them as a parent would.[57] Subsequently, a symbiotic relationship can form where the spouse needs the agoraphobic as much as the agoraphobic needs the spouse. In one case, the husband of an agoraphobic developed a paranoid psychosis one month after the successful treatment of his wife. He recovered shortly after his wife resumed her agoraphobic ways.[55]

Other family members can also hamper the agoraphobic's progress by overprotection. They may insist on accompanying the agoraphobic on forays outside the "circle of safety,"[32] thus keeping the patient from coming to terms with the disorder. To prevent such problems, Hafner recommends that members of an agoraphobic's immediate family also undergo treatment. This therapy should include education as to the nature of agoraphobia, advice on dealing with the effect the disorder has on family life, and help in coping with the changes that will occur after the agoraphobic's symptoms improve.[57]

Agoraphobics can now turn to a number of organizations for help. The most prominent of these is TERRAP, mentioned earlier. TERRAP was organized in 1964 by Hardy and several other former agoraphobics. Since that time, Hardy and other TERRAP therapists have treated 5,000-6,000 agoraphobics through their 43 treatment centers located in 26 states. The treatment usually consists of exposure *in vivo*, conducted in groups. Another well-known organization that specializes in treating agoraphobics is the Phobia Clinic, White Plains Hospital Medical Center, New York. The treatment at White Plains is termed "contextual therapy," and was developed by clinic director Manuel D. Zane.[58] Contextual therapy is very similar to exposure therapy. The therapist travels with the agoraphobic to a setting where the phobic reaction occurs. At the setting, the therapist works with the patient to help replace anxious feelings with more constructive ones. They then make as many trips as are needed for the phobic reaction to be extinguished.

Despite the efforts of the organizations cited here, and other groups listed in Table 1, most agoraphobics remain untreated. They find that they cannot drive to the treatment center, or that treatment is too expensive, or unavailable locally. Some 60 to 70 percent of the agoraphobics that contact TERRAP remain afflicted for these reasons.[59] TERRAP director Hardy is now forming a corps of improved agoraphobics who can provide inexpensive help to those unable to visit a TERRAP center.[59] But it will take further bold and creative steps on the part of those in a position to help before the many victims of this disorder can lead normal lives.

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