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Research Review

ANXIETY ACROSS THE LIFE SPAN: EPIDEMIOLOGICAL EVIDENCE AND TREATMENT DATA

Richard Balon, M.D.*

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INTRODUCTION

Eight reviewed articles present some interesting data about the following: 1) Psychopathology, pathogenesis, and course of anxiety disorders such as the influence of various factors such as childhood sexual abuse and parenting on lifetime pathology, the overlap between anxiety and attention deficit disorder, the relationship between alcohol consumption and symptoms of anxiety and depression, and the "effect" of age on symptoms of anxiety and depression, and 2) treatment issues such as antecedents of recovery in social phobia; recovery rates and efficacy of psychological treatments for generalized anxiety disorder; and the efficacy of cognitive behavioral therapy, imipramine, or both for the treatment of panic disorder.

EARLY SEXUAL ABUSE AND LIFETIME PSYCHOPATHOLOGY: A CO-TWIN-CONTROL STUDY. Dinwiddie S, Heath AC, Dunne MP, Bucholz KK, Madden PAF, Slutske WS, Bierut LJ, Statham DB, Martin NG: *Psychol Med* 2000; 30:41–52

Awareness of the extent and sequelae of child sexual abuse (CSA) has increased lately. Various symptoms and syndromes have been reported in persons with a history of child sexual abuse. However, many studies of psychopathology and CSA suffer from methodological limitations. Furthermore, environmental factors associated with increased risk for CSA, such as significant family violence or conflict, or presence of a stepfather, are known to influence the risk of later psychological maladjustment and psychopathology even in the absence of CSA. Other confounding variables in this relationship could be constitutional factors. One of the methods of untangling this complicated relationship is the twin study method.

This epidemiological study was designated to determine lifetime prevalence of psychiatric disorders among twins who reported childhood sexual abuse. Specifically, diagnoses of alcohol abuse/dependence, major depression, anxiety disorders, including panic disorder and social phobia, and conduct disorder were established by using the DSM-III-R diagnoses. The rates of psychiatric illness in these twins were compared to the rates of psychiatric disorders among non-abused co-twins.

The total number of subjects interviewed over the phone included 1,341 monozygotic pairs (940 female and 401 male), 776 dizygotic pairs (540 female and 236 male), and 604 opposite-sex twin pairs, plus data on 553 "singleton" twins (i.e., where data were available on only one member of a twin pair). The trained lay interviewers obtained lifetime history of psychiatric symptoms to generate DSM-III-R diagnoses. They also asked one question about CSA: "Before age 18, were you ever forced into sexual activity, including intercourse?"

The prevalence of reported CSA in this sample was 5.9% among women and 2.5% among men. Elevated rates among abused individuals were seen for all disorders (alcohol abuse/dependence, major depression, anxiety disorders including panic disorder and social phobia, and conduct disorder) in women and for all disorders except social phobia among men. Also, the association between CSA and reporting a serious suicide attempt was strong in both genders, while lifetime major depression and any suicidal ideation were even more strongly associated with reported CSA in men than women, as was the case also for panic disorder. Abused women, but not men, were also more likely to report social phobia. When comparisons were restricted to non-abused co-twins, no differences in psychopathology were observed. However, rates of major depression, conduct disorder, and suicidal ideation were higher if both co-twins were abused than if the respondent alone reported CSA.

The authors pointed out several limitations of this

Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, Michigan

*Correspondence to: Richard Balon, UPC-Jefferson, 2751 East Jefferson, number 200, Detroit, Michigan 48207.
E-mail: rbalon@wayne.edu

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study: 1) the assessment instrument used was originally designed to assess alcoholism and did not specifically address other forms of psychopathology than those mentioned (e.g., personality disorders or PTSD were not diagnosed); 2) identification of CSA was based on self-report only; 3) the definition of CSA required coerced sexual activity (some responders may have reported only CSA involving physical force); and 4) analyses showed that rates of psychopathology were increased among abused respondents from families where the respondent's twin sister had also been abused, thus limiting the generalizability of matched-pairs comparisons of abused-discordant twins.

The authors conclude that CSA is a potentially devastating life experience with deleterious effects and an increased risk of psychopathology development. They also felt that the twin study approach of the association between CSA and psychopathology, by allowing for estimation not only of genetic but also of shared environmental effects, can deepen the understanding of how multiple factors of varying degrees of specificity can interact to result in mental illness.

PARENTING AND ADULT MOOD, ANXIETY AND SUBSTANCE USE DISORDERS IN FEMALE TWINS: AN EPIDEMIOLOGICAL, MULTI-INFORMANT, RETROSPECTIVE STUDY. Kendler KS, Myers J, Prescott CA: *Psychol Med* 2000; 30:281–294

The authors of this study pointed out that several psychodynamic schools as well as the influential attachment theory developed by Bowlby have posited that the etiology of most psychiatric disorders lies in deficiencies in parenting. In an epidemiological twin study, Kendler et al. attempted several major questions related to this issue:

1. What is the magnitude of the association between retrospectively reported parenting behavior and the risk in offspring for a range of common psychiatric and substance use disorders?
2. How much of this association is mediated through predictors of parenting and therefore may not be causal?
3. Is maternal or paternal parenting behavior more influential in the risk for psychiatric and drug use disorders in daughters?
4. What is the level of specificity of the association between individual disorders and particular parenting dimensions? How much does the observed association decline when other disorders and or parenting dimensions are included in the analysis?
5. How commonly are interactions observed in the prediction of risk for disorder in offspring either between different parenting dimensions or between maternal and paternal parenting?
6. What proportion of the observed correlation in risk for psychiatric or substance use disorders in siblings is likely due to their shared experience of being parented?

In several telephone interview waves over 9 years, the authors interviewed female-female twins from Virginia Twin Registry born between 1934 and 1971, and most of their biological parents. Parenting was assessed by the Parental Bonding Instrument [Parker et al., 1979] and three meaningful factors, from which three scales were derived, were determined: coldness (C), protectiveness (P), and authoritarianism (A). Psychiatric and substance use disorders were diagnosed by using adaptation of the SCID interview with two exceptions: 1) phobia was assessed by using an adaptation of the DIS interview and 2) a 1-month duration rather than 6-month minimum duration of illness for generalized anxiety disorder (GAD) was used.

The findings related to the major research questions outlined above were as follows:

1. Most of the observed associations between parenting and risk of certain illnesses (major depression, phobia, GAD, alcohol dependence, panic, drug abuse, drug dependence, and bulimia) were significant. However, the magnitude of the associations was modest. Averaged across the eight disorders, the strongest associations were for C followed by A, and the weakest association was for P. GAD and phobias were significantly associated with maternal and paternal C, A, and P. Major depression (MD) and panic were significantly associated with all parenting dimensions except paternal P. Bulimia was significantly associated only with maternal C.
2. Parental coldness was predicted by a parental history of MD, panic disorder, and GAD, and the authors felt that the association between parental coldness and these disorders in their children could be mediated through genes rather than parenting. They also felt that the association between parenting behavior and psychiatric and substance use disorders in the offspring was only in part causal.
3. This study found no significant difference across any parenting dimension for any disorder with respect to parenting behavior of mothers vs. fathers. For women, the parenting received from fathers and mothers is equally important in influencing risk for psychiatric and substance use disorders.
4. Nearly all associations between parenting and illness in offspring appeared to be mediated through the levels of parental C, with the exception of GAD and phobia, where P had a significant independent contribution. The authors concluded that much of the impact of parenting on risk for psychiatric and substance use disorders in women may be largely mediated through an increase in risk for major depression, phobia, and GAD.
5. No significant positive interactions were found for parental C for any of the eight disorders examined.
6. Parenting appears to have a consistent but modest impact on risk for most disorders. Correlation in liability to the psychiatric and substance use disorders due to sibling shared experiences of being parented is very modest.

As the authors pointed out, this study had numerous

limitations: 1) studying females only; 2) not using the full PBI; 3) retrospective character; 4) combination of three informants led to obscuring the impact of a specific informant; 5) only twin families were used; 6) parents were examined through self-report, while siblings were examined through interview; and 7) only general dimensions of parenting were studied.

In summary, in women, parenting behavior, especially levels of coldness, is probably causally related to the risk for a broad range of adult psychiatric disorders. The impact of parenting on substance use disorders may be largely mediated through their comorbidity with major depression, phobias, and GAD. In general population samples, the association of poor parenting with psychiatric illness is modest, largely nonspecific, and explains little of the observed aggregation of these disorders in families.

CHILDHOOD ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN ADULTS WITH ANXIETY DISORDERS. Mancini C, Van Ameringen M, Oakman JM, Figueiredo D: *Psychol Med* 1999; 29:515–525

In childhood, attention deficit hyperactivity disorder (ADHD) frequently co-occurs with conduct disorder, mood disorders, and anxiety disorders. Main symptoms of ADHD may persist through adolescence and into adulthood, and the comorbidity also may persist into adulthood. However, there is a large overlap between the symptoms and clinical presentations of ADHD and comorbid disorders, which complicates the interpretation of comorbidity. Many ADHD patients meet criteria for GAD, social phobia, or panic disorder. Also, the risk for anxiety disorders was reported to be greater among relatives of children with ADHD than among relatives of normal children and greater still among relatives of children with both ADHD and anxiety disorders. The ADHD and anxiety disorders tend to co-segregate in families.

Given the association between ADHD and anxiety disorders both in terms of comorbidity and family studies, the authors of this study attempted to establish the prevalence of childhood ADHD in an anxiety disorder clinic sample and to examine the effect of a childhood history of ADHD on anxiety disorder symptomatology. They evaluated 149 consecutive admissions/referrals to a university affiliated Anxiety Disorders Clinic. Patients surpassing the cut-off score of 36 on the 25-item subscale of the Wender Utah Rating Scale [Wender et al., 1981; Ward et al., 1993] were asked to be interviewed using a structured interview (SCID). Authors were able to interview 29 of 36 patients who met the criteria for Adult ADHD based on Wender's criteria [Ward et al., 1993]. In addition to SCID, the patients completed a number of self-reported measure of anxiety and depression (e.g., Fear Questionnaire, State-Trait Anxiety Inventory, Beck Depression Inventory, Anxiety Sensitivity Index, Yale-Brown Obsessive Compulsive Scale, and Liebowitz Disability Self-rating Scale).

Even when the possible inflation of retrospective accounts of ADHD was considered, there was still a significantly higher prevalence of ADHD in the retrospective reports of adults with anxiety disorders (15%) than would be expected by chance (4%). Furthermore, of those who meet retrospective criteria for ADHD, 45% (13 of 29) continue to meet diagnostic criteria for ADHD as adults. People with social phobia as a primary diagnosis endorsed a childhood history of ADHD symptoms at a higher rate than did people with panic disorder as a primary diagnosis. People with obsessive-compulsive disorder as a primary diagnosis were intermediate between these two groups. Higher reporting of childhood ADHD symptomatology was modestly associated with earlier onset of the primary anxiety disorder and having a greater number of non-ADHD psychiatric diagnoses in general. It was also found to be associated with a greater number of anxiety disorder diagnoses, more mood disorder diagnoses, and more substance and alcohol abuse disorder diagnoses. Patients who reported a history of ADHD tended to report more symptoms but no more functional impairment than those patients who did not report childhood ADHD symptoms. The authors also concluded that it is probably a childhood history of ADHD that predicts increased psychiatric distress as adults, rather than having a current diagnosis of adult ADHD. The authors also thought that their finding of a high rate of ADHD in the history of people with adult anxiety disorders, especially among those diagnosed with social phobia, is consistent with the contention that childhood anxiety disorders may present like ADHD but be quite separate disorders.

The authors pointed out that the limitation of their study was the lack of collateral information.

NON-LINEAR RELATIONSHIPS IN ASSOCIATIONS OF DEPRESSION AND ANXIETY WITH ALCOHOL USE. Rodgers B, Korten AE, Jorm AF, Jacomb PA, Christensen H, Henderson AS. *Psychol Med* 2000; 30:421–432.

The comorbidity of alcohol use disorders with mood and anxiety disorders (major depression, dysthymia, mania, panic disorder, agoraphobia, social phobia, OCD, PTSD, and GAD) is well established. However, relatively little is known about anxiety and depression across the full continua of alcohol consumption, from abstinence to heavy drinking, and problems associated with drinking.

The authors analyzed a self-completed questionnaire (filled in the presence of the interviewer) of randomly selected men (1,294) and women (1,431) in Canberra, Australia. The questionnaire included various measures of anxiety and depression. It also included the Australian version of the WHO Alcohol use Disorder Identification Test (AUDIT), a ten-item instrument that covers recent alcohol intake, depen-

dence, and consequences of drinking with respect to the reactions of others, amnesia, and injury.

The authors found that men drank more than women and reported more problems associated with drinking. Younger people reported more problems associated with drinking than did older people and had higher AUDIT total scores. The authors also found relationships of high levels of alcohol use and associated problems with symptoms of anxiety and depression. The relationships appeared weaker in those aged 60 and over compared with younger persons. This is consistent with reports that anxiety disorders are not associated (or may be inversely associated) with alcoholism in the elderly.

The most interesting finding was that non-drinkers and heavy drinkers had higher depression and anxiety scores than those who drank at low consumption level and a similar U-shaped relationship was observed for negative affect scores and alcohol consumption. This all mirrors the established finding of a U-shaped relationship between mortality and alcohol consumption. The U-shaped relationship of psychological distress with alcohol consumption was still evident after the exclusion of former heavy drinkers and those who reported ever having drinking problems.

The authors entertained several explanations for their findings: a) moderate drinking may be somewhat protective in relation to anxiety and depression; b) negative affect influences drinking, suggesting that high depression and/or anxiety can lead to either abstinence or to increased consumption; and c) third factors could be implicated in the negative affect of both abstainers and heavy users (e.g., financial hardship could lead to either heavy drinking or abstinence).

The limitations of this study were the absence of longitudinal data, the inability to determine directly whether ex-drinkers could account for the high symptom levels in current non-drinkers, and the lack of using specific diagnoses.

The authors concluded that a full account of the comorbidity of alcohol use disorders and other mental disorders should acknowledge the possibility of nonlinear associations and employ continuous as well as discrete measures. Furthermore, more attention should be given to abstainers as a group at risk for mood and anxiety disorders. Finally, it is possible that psychosocial factors evident in the early adulthood (or before) play a role in the established U-shaped relationship between alcohol consumption and mortality.

DOES OLD AGE REDUCE THE RISK OF ANXIETY AND DEPRESSION? A REVIEW OF EPIDEMIOLOGICAL STUDIES ACROSS THE ADULT LIFE SPAN. Jorm AF: *Psychol Med* 2000; 30:11–22

This interesting literature review article examined differences across the adult life span in the risk of anxiety and depression disorders and symptoms. The author searched for studies examining the prevalence, incidence or level of anxiety, depression, or general distress across the adult life span. Many studies show a rise in the prevalence of anxiety and depression across age groups, followed by a drop, but with no consistent peak age (there are actually only two anxiety symptoms studies that do not show consistent results).

The author also speculated what could lie behind a possible, underlying age effect, since there is some evidence that there may be an age-related decrease in risk for anxiety and depression once other risk factors are controlled. The three possible explanations are a) decreased emotional responsiveness with age; b) learned increased emotional control in older people; and c) "psychological immunization," i.e., people develop resistance to adverse life events through repeated exposure.

There is no clear answer about a decreased risk of anxiety and depression associated with aging. Longitudinal studies are definitely needed.

RECOVERY RATES IN GENERALIZED ANXIETY DISORDER FOLLOWING PSYCHOLOGICAL THERAPY: AN ANALYSIS OF CLINICALLY SIGNIFICANT CHANGE IN THE STAI-T ACROSS OUTCOME STUDIES SINCE 1990. Fisher PL, Durham RC: *Psychol Med* 1999; 29:1425–1434

The aim of this paper was to reach a better understanding of the value of psychological therapy in treating a psychiatric disorder that might reasonably be said to lie at the heart of the general neurotic syndrome, GAD. The authors analyzed six randomized controlled trials of psychological therapy with GAD (total patient population of 404), which used DSM-III-R or DSM-IV diagnostic criteria. The authors computed the clinical significance of treatment effect, using standardized Jacobson criteria [Jacobson and Truax, 1991], on a measure of general vulnerability to anxiety, the trait version of State-Trait Anxiety Inventory (STAI-T). Each patient was allocated to one of four outcomes: worse, unchanged, improved, or recovered. The proportion of patients in each category was calculated for treatment condition in each study and also for aggregate data across types of treatment.

The six analyzed studies compared a) cognitive-behavior therapy (CBT) and behavior therapy (BT); b) applied relaxation (AR), cognitive therapy (CT), and the two combined; c) CT, CBT, BT, and placebo in a large group psychoeducational format; d) CBT, AT, and Rogerian non-directive therapy (ND); e) analytical psychotherapy (AT)-high and low contact, CT-high and low contact, and anxiety management training; and f) applied relaxation plus self-control desensitization (AR/SCD), CT, and the two combined.

Very few patients were worse at either post-treatment or follow-up, although a significant majority remained unchanged (45% at post-treatment and 36% at follow-up). The percentage of patients who improved but remained within the dysfunctional distribution was

approximately one quarter of all treated patients at both post-treatment and follow-up. The overall figures suggested that approximately 60% of patients made some form of significant improvement following psychological therapy but, on average, slightly less than 40% can be considered to be recovered in terms of STAI-T. Two treatment approaches (individual behavior therapy and analytical therapy) did very poorly, in fact were broadly comparable to the waiting list condition (recovery rates less than 20% at the end of treatment with less than 10% maintaining recovery during follow up; virtually no patients achieved recovery during the follow-up and overall recovery rates at follow-up were less at the end of treatment). Two other treatments, individual CBT and applied relaxation, did relatively well. Approximately 50% of patients were recovered at the end of treatment and the majority of patients sustained recovery during the follow-up. Between these contrasting levels of treatment efficacy were three therapy approaches, group CBT, group BT, and nondirective therapy, with an intermediate pattern of results.

There were several limitations of this study: a) additional pharmacotherapy or psychotherapy given during the follow-up, b) restricted range of symptoms measured by the STAI-T, and c) small number of studies.

GAD is a difficult disorder to treat effectively. The most effective psychological treatments seem to be individual CBT or applied relaxation; these therapies target the chronic muscle tension and excessive worry that are cardinal features of this disorder.

ANTECEDENTS OF THE RISK OF RECOVERY FROM DSM-III-R SOCIAL PHOBIA. DeWitt DJ, Ogborne A, Offord DR, MacDonald K: *Psychol Med* 1999; 29:569–582

Individuals afflicted from social phobia endure a heavy burden of suffering. Social phobia is linked with functional impairment in the areas of school, family, and employment. Systematic investigations of the course and chronicity and predictors of recovery of social phobia are rare. This study focused on a) the description of the natural course of DSM-III-R social phobia in the general population, and specifically, the median length of time of the illness and the peak periods of risk of recovery, and b) salient antecedents of the risk of recovery from social phobia. Retrospective data were obtained from 1,027 individuals participating in a large population health survey in Ontario, Canada. The diagnostic data were obtained from the World Health Organization's Composite International Diagnostic Interview. other questions, including issues such as childhood physical abuse and parental psychiatric status, were asked.

The lifetime prevalence rate of social phobia among persons aged 15 to 64 years was 13.7%, with median age of onset of 12.7 years. Approximately 9% of diagnosed individuals reported four or more social fears, 16.5% reported three fears; 31.7% reported two fears, and 42.4% reported one fear. More than one third (37.5%) reported a pure public speaking fear only. The median length of recovery was 25 years, and just over 48% of respondents had not recovered from their illness by the survey date. Preliminary analysis indicated high colinearity between parental conflict and parental separation.

Age at onset of social fears emerged as the most powerful predictor of recovery. Individuals reporting an onset past the age of 13 years were 8.59 times more likely to recover compared to those with an onset before the age of 7 years. Individuals endorsing one social fear were 3.11 times more likely to recover compared to those endorsing four or more fears. The number of social fears was a better predictor than the type of social phobia. There was an increased risk of recovery among respondents with one or no siblings (however, having four or more siblings also predicted increased risk of recovery) and a small town of residence when growing up. Individuals not reporting sexual abuse were 1.55 times more likely to recover than those reporting severe abuse. Subjects reporting an absence of chronic health problems were nearly five times more likely to recover. Absence of major depression was associated with a nearly three-fold increase in the risk of recovery. Individuals who reported an onset of major depression prior to the onset of their social phobia were over three times more likely to recover compared to those who reported an onset of depression to follow their illness (social phobia). Finally, chances of recovery were reduced for those contacting health or social professionals about their social fears (those may be more ill). Interestingly, there was also no significant relationship for alcohol dependence.

The limitations of this study were a) the use of retrospective data (lack of measure for true persistence of social phobia, error associated with respondent recall, and reliability issues) and b) lack of measures of social competency.

The authors suggest that the assessment and treatment should begin early and should include more intensive therapies for those who develop multiple fears (i.e., a generalized phobia). Special interventions may be necessary to treat persons who also have comorbid chronic health problems and major depression.

COGNITIVE-BEHAVIORAL THERAPY, IMIPRAMINE, OR THEIR COMBINATION FOR PANIC DISORDER. A RANDOMIZED CONTROLLED TRIAL. Barlow DH, Gorman JM, Shear MK, Woods SW: *JAMA* 2000; 283:2529–2536

The principal authors of this study point out that despite the proven efficacy of both drug and psychosocial treatments for panic disorder and some emerging evidence on the possible synergistic effects of these approaches, particularly on phobic behavior, studies of medication and psychosocial approaches have, until recently, run on parallel and sometimes hostile tracks.

The authors assembled a team of four investigators, two committed to each approach, to undertake a comparative study that would determine optimal treatment for panic disorder with or without mild agoraphobia. They conducted a randomized controlled trial that compared cognitive behavioral therapy (CBT) (77 patients), imipramine up to 300 mg/day plus medication management (83 patients), the combination of CBT and imipramine (CBT + imipramine) (65 patients), pill placebo plus medication management (24 patients), and CBT + placebo (63 patients) for panic disorder. Patients were treated weekly for 3 months (acute phase). Responders were then seen monthly for 6 months (maintenance phase) and then followed up for 6 months after treatment discontinuation. The treatment response was assessed using the Panic Disorder Severity Scale (PDSS) and Clinical Global Impression Scale (CGI).

Therapists in this study were doctoral level clinicians who underwent extensive training and certification supervised by one of the sites. Pharmacotherapists were experienced psychiatrists. Imipramine and placebo were administered in a double-blind, fixed flexible dose design. The starting dose of imipramine was 10 mg/day with an increase of 10 mg every other day, and more rapid escalation after 50 mg/day was reached. Blood levels of imipramine were obtained at weeks 6 and 12.

Both CBT and imipramine were significantly superior to placebo for the acute treatment phase as assessed by the PDSS, but the responses were not significantly different for the CGI. Among responders, imipramine produced a response of higher quality as measured by PDSS. After 6 months of maintenance, both imipramine and CBT were significantly more effective than placebo for both the PDSS and CGI. The follow-up analyses showed trends favoring CBT over imipramine. The combination of CBT and imipramine was not significantly better than CBT and placebo but was better than CBT alone. Responders to imipramine, with or without CBT, fared significantly worse in the no-treatment follow-up period than those who received CBT alone or CBT + placebo.

The results demonstrate that both imipramine and CBT are better than pill placebo for treatment of panic disorder. Imipramine produced a superior quality of response, but CBT had more durability and was somewhat better tolerated. Among those who did well with either treatment, patients receiving imipramine responded more completely; however, patients who received CBT alone maintained their improvement significantly better. Acute co-administration of imipramine and CBT resulted in limited benefit over monotherapy. Surprisingly, the addition of CBT to imipramine did not mitigate relapse following medication discontinuation; addition of imipramine appeared to reduce the long-term durability of CBT. More work is needed to elucidate these somewhat confusing findings.

This study had several limitations: a) only patients with limited avoidance were included; b) a tricyclic antidepressant and not an SSRI was used, although an SSRI would probably be better tolerated; c) the therapeutic potential of imipramine was possibly underestimated (plasma level of imipramine/desipramine of 150 mg/mL may be optimal, while the dose of at least 200 mg/day was pushed in this study), d) possible use of additional medication, and e) lack of optimal strategy for tapering imipramine. Nevertheless, this is a landmark treatment combination study.

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