Association Between Early or Later Onset of Substance Use and Psychiatric Disorders in Women

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INTRODUCTION

The comorbidity of psychiatric disorders with drug addiction has been established, but only recently has the importance of this relationship been emphasized. Rates of comorbidity vary according to factors relevant to recall and those that are inherent in the method of assessment. Recall factors include the salience, timing, and severity of symptoms. Assessment factors include the reliability of the diagnostic assessment chosen, the method of data ascertainment (computer v. paper-and-pencil), and the diagnostic system on which the assessment is based (e.g., the various versions of the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition* [*DSM-III*]*; DSM-III-R* [*Third Edition, Revised*], or *DSM-IV* [*Fourth Edition*] [American Psychiatric Association 1980, 1987, 1994]). Sample characteristics, such as general population or in-treatment samples, men or women, older or younger subjects, and ethnicity, along with other individual risk factors, have also been shown to affect rates of comorbidity (Regier et al. 1990; Ross et al. 1988; Weissman et al. 1980; Mirin et al. 1988; Mirin and Weiss 1986; Weiss et al. 1986; Rounsaville et al. 1982; Kosten and Rounsaville 1986; Mirin et al. 1991; Hesselbrock et al. 1985; Khantzian and Treece 1985; Powell et al. 1982; McLellan et al. 1983; Croughan et al. 1982; Jainchill et al. 1986; Hasin et al. 1988; Rounsaville et al. 1991).

The Epidemiologic Catchment Area (ECA) Study found that rates of psychiatric disorders were higher among substance users than among nonusers for every category of *DSM-III* substance abuse or dependence (Regier et al. 1990). Overall, 53 percent of persons in the ECA with substance use disorders met the criteria for one or more psychiatric conditions. Similarly, the National Comorbidity Survey (NCS) showed

that *DSM-III-R* psychiatric disorders are more common among substance abusers than expected (Kessler et al. 1994). According to the NCS, about one-half of the individuals with a past-year substance use disorder (47 percent) had both substance abuse/dependence and another mental disorder—more than double the rate for the overall population.

Particularly among treatment-seeking substance abusers, psychiatric comorbidity has been found to be commonplace (Rounsaville et al. 1982; Rounsaville et al. 1991). In samples of persons seeking treatment, rates of comorbid psychiatric diagnoses have been estimated at almost 65 percent for the past year and 78 percent over the client's lifetime (Ross et al. 1988). This raises the question of reasons for higher rates of psychiatric illness among treatment-seeking substance abusers. Grant (1997) recently showed that depression is higher among treatment-seeking substance abusers and much less pronounced among those not seeking treatment. The causal link, if any, between drug use and a psychiatric disorder remains murky, especially where details on the progression from one illness to another are concerned. Furthermore, research should be conducted to improve the recognition of the comorbidity among abusers and to improve prevention and treatment approaches.

Lehman and colleagues (1989) proposed several theoretical constructs: mental illness causing substance dependence, substance dependence causing a mental disorder, each diagnosis occurring independently, and both problems being caused by some common factor. For example, posttraumatic stress disorder (PTSD) has been found to both precede and follow substance abuse (Cottler et al. 1992). Mood and anxiety symptoms observed in active substance users frequently improve with abstinence (Weddington et al. 1990; Schuckit 1986; Rounsaville et al. 1986). This implies that some cases of coexistent depression and anxiety may be related to the use of psychoactive substances and has led to controversy about when to start treatment for comorbid psychiatric conditions in substance abusers. Recent evidence has supported the idea of treating coexisting psychiatric disorders among substance abusers early in treatment, especially in the case of coexisting depression (Nunes et al. 1993, 1994; Batki et al. 1987; Woody et al. 1982; Dorus et al. 1989; Mason and Kocsis 1991) and perhaps anxiety disorders as well (Kranzler et al. 1994; Malcolm et al. 1992). Underrecognition of symptoms continues to be one of the major problems that has occurred in both understanding and treating these conditions.

Despite the proliferation of papers linking psychiatric disorders with substance abuse, the extent of this association among women has not been fully addressed in the literature (Alexander 1996). Studies from Brooner and colleagues (1997) emphasize the importance of providing therapeutic interventions that address the psychiatric comorbidity. Using behavioral interventions in conjunction with pharmacotherapy may significantly improve the outcomes for patients with comorbid psychiatric disorders.

In the past several years attention has been placed on subtypes of alcoholics. Babor and colleagues (1992) identified two distinct types of alcoholics who differ with respect to a variety of defining characteristics, including age of onset—those who are characterized by later onset, with less severe dependence and fewer alcohol-related problems, and those who are characterized by early onset, with greater severity of dependence and more extreme alcohol-related problems. These subtypes of alcoholics have been identified among both men and women.

The study described in this chapter advances the knowledge of the comorbidity literature by addressing the consequences of substance abuse among both treated and untreated users, by deleting the confounder of gender to focus only on women, and by stratifying the sample by early or late onset of substance abuse.

METHODS

Sample

The women included in these analyses were drawn from two separate NIDA-funded studies of illicit substance users in the St. Louis area with varying substance use patterns and severity of problems. The studies were conducted from 1990 to 1994. The first sample (n=204) came from the Substance Abuse and Risk for AIDS (SARA) study, a longitudinal study of substance abusers who had recently been admitted to treatment or who resided in one of two shelters for women and who were reforming prostitutes or were in recovery from substance abuse (Cottler et al. 1991). The second sample (n=134) was obtained from the Efforts to Reduce the Spread of AIDS (ERSA) study (Cottler et al. 1993, pp. 205-218; Cottler et al. 1995, pp. 233-248). This longitudinal demonstration study sought to improve drug abuse treatment in the most vulnerable, high-risk areas of St. Louis. ERSA subjects were obtained

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through street outreach and thus represent out-of-treatment substance abusers. The followup rate for both studies was in excess of 90 percent; in fact, ERSA achieved a 96.6 percent followup at 18 months (Cottler et al. 1996). The samples were pooled to increase the ability to detect differences; pooling was possible because the two studies used nearly identical diagnostic assessments. There was no overlap in subjects across the two studies, a total of 338 women.

Interview

Respondents were questioned in person by interviewers who had undergone extensive training on administration of the interviews and on study protocols. The informed consent procedure, cleared by both the Washington University Institutional Review Board and the State of Missouri Department of Drug and Alcohol Abuse, advised potential respondents of the confidentiality of their responses. Participation was further protected by a NIDA Certificate of Confidentiality.

The interview included an assessment of substance abuse and dependence for alcohol, amphetamines, cannabis, cocaine, hallucinogens, inhalants, opiates, PCP (phencyclidine), sedatives, and tobacco. The SARA study used the American Psychiatric Association's Diagnostic Interview Schedule (DIS, Version III-R); the ERSA study used the World Health Organization's Composite International Diagnostic Interview-Substance Abuse Module (CIDI-SAM). The differences between these instruments are minimal. The CIDI-SAM elicits information about specific withdrawal symptoms as well as the psychological, physical, and social consequences of drug use; the DIS obtains the same information in a briefer form. Because these assessments are from the same family of instruments (Cottler and Compton 1993) and the core components are identical, they are compatible for analyses. Histories of lifetime psychiatric symptoms were obtained by the DIS, with the following sections included: depressive disorders, generalized anxiety, panic, phobic disorders, antisocial personality disorder (ASPD), PTSD, and pathological gambling.

Stratification of Sample

For these analyses women were divided into early and later substance use groups, according to the age of onset of the first drug use

(alcohol and tobacco excluded) and the onset cluster years. *Age of onset* refers to the age at which a respondent first used an illicit drug, as reported on the SAM/DIS. *Onset cluster years* refers to the span of years in which an individual's drug repertoire began. In addition, a second age-of-onset term, the *restricted age of onset,* is used to indicate this age of onset limited to the first use of cocaine or opiates or "other drugs" if cocaine/opiates were not used. On the basis of these combined data, the sample was grouped into onset indexes of either "early" or "later" drug use.

As shown in table 1, 84 percent of the sample reported using cocaine, with or without other drugs; 53 percent reported using opiates, with or without other drugs; and 9 percent reported using drugs other than cocaine/opiates. On the basis of the grouping criteria described above, 55 percent of the sample were characterized as early users and the remaining 45 percent as later users. Early users included 46 percent of the sample whose drug use started, on average, by 15.7 years of age—the earliest age of onset of the four groups shown in table 1. These same women had used cocaine or opiates by age 20.1 for an average onset cluster span of 4.4 years. Early users also consisted of women who did not use cocaine or opiates but whose onset span for other drugs was short (within 6 months). Women characterized as later users included those who used other drugs with cocaine or opiates, those who did not use their first drug until at least 18 years of age, and those whose onset span was longer than the others.

TABLE 1. *Stratification of SARA/ERSA drug-using women (n=338)*

Substance Used			Sample Size		Age of Onset of Any Drug Use (Years)	Restricted Age of Onset (Years)	Onset Cluster Years	Onset Index*
Cocaine	Opiates	Other Drugs	Number	Percent				
+	+	+/–	156	46	15.7	20.1	4.4	Early
+	–	+/–	127	38	18.8	25.4	6.6	Later
–	+	+/–	24	7	18.0	21.8	3.8	Later
–	–	+	31	9	17.4	17.9	0.5	Early

*Considers cluster and onset age

KEY: SARA/ERSA=Substance Abuse and Risk for AIDS/Efforts to Reduce the Spread of AIDS

Analyses

The authors performed analyses using SAS version 6.12. For categorical data, chi-squared tests were employed. Student's *t*-tests were used to compare means.

RESULTS

Demographics

As shown in table 2, the mean age of all women in the sample was 31.9 years (standard deviation [SD]=6 years). Of this sample, 67 percent were African-American, 14 percent were married at the time of the interview, 77 percent had one or more children, 45 percent had attained less than a high school education, 70 percent were unemployed, and 52 percent lived in their own houses or apartments. The early users were differentiated from the later users by age, racial mix, and current living arrangement. Specifically, the early users were slightly older than the later users at the time of the interview (33.0 years v. 30.5 years, SD=6 years) and were more likely to be racially diverse (53 percent v. 83 percent African-Americans) and living in their own houses or apartments (59 percent v. 43 percent). With these exceptions, the two groups were comparable in their sociodemographic characteristics.

Patterns of Substance Use

The use of all substances except alcohol, cocaine, and PCP was found to be statistically more prevalent among early users than among later users. As seen in table 3, for more than half of the drug categories, the rates among early users were more than double those of the later group. Although not shown in the table, injection drug use was more than three times as prevalent among early users as among later users (68 percent v. 22 percent).

Although rates of use were higher among early users than among later users, there was no difference among the various drugs in rates of dependence between the two groups, except for alcohol, in which case early users were more likely to be dependent (table 3). Furthermore, as shown in table 4, women categorized as early users were more likely to have experienced consequences of use of any drug from 2 to 4 years earlier than women categorized as later users (average age 22.4 years for

TABLE 2. *Sociodemographic characteristics of SARA/ERSA drug-using women*

Characteristics	Sample Size (N=338)		Substance Use Status	
	Number	Percent	Early Users (N=187)	Later Users (N=151)
Mean age in years (SD)	31.9 (6)		33.0 (6)	30.5* (6)
			Percent	Percent
Age				
24 years or younger	34	10	7	13
25-34 years	180	53	45	64*
35 years or older	124	37	48	23*
Ethnicity				
African-American	225	67	53	83
Other	113	33	47	17†
Marital status				
Currently married	49	14	17	11
Not married	289	86	83	89
Children				
No children	77	23	22	24
One or more children	261	77	78	76
Education level				
Less than high school	153	45	44	47
High school or more	185	55	56	53
Employment status				
Unemployed	237	70	66	75
Employed	100	30	34	25
Current living arrangements				
In own house or apartment	174	52	59	43
Someone else's house/ shelter/street	162	48	41	57*

*p 0.01
†0.01<p 0.05

KEY: SARA/ERSA=Substance Abuse and Risk for AIDS/Efforts to Reduce the Spread of AIDS; SD=standard deviation

TABLE 3. *Substance use and dependence among SARA/ERSA drug-using women (percent)*

Drugs	Early Users (N=187)		Later Users (N=15)		p	
	Use	Dependence*	Use	Dependence*	Use	Dependence*
Alcohol	81	62	74	40	NS	0.001
Cannabis	91	33	73	25	0.001	NS
Amphetamines	60	41	27	27	0.001	NS
Sedatives	66	34	21	25	0.001	NS
Cocaine	83	73	84	77	NS	NS
Opiates	83	58	16	71	0.001	NS
PCP	22	34	16	46	NS	NS
Hallucinogens	39	14	9	8	0.001	NS
Inhalants	10	22	1	50	0.001	NS

*DSM-III-R dependence, lifetime

KEY: SARA/ERSA=Substance Abuse and Risk for AIDS/Efforts to Reduce the Spread of AIDS; NS=not significant; PCP=phencyclidine

TABLE 4. *Progression of symptoms of drug dependence among SARA/ERSA drug-using women*

	Mean Age at Onset of Symptoms		
Symptom	Early Users (N=187)	Later Users (N=151)	p
Consumption greater/longer than intended	21.9	24.8	0.0007
Persistent desire/unsuccessful efforts to cut down	22.5	25.6	0.0001
Excessive time spent using/getting/recovering from effects	20.9	24.2	0.0001
Use with increased risk of injury	20.2	23.5	0.0002
Given up/reduced important activities	23.7	27.2	0.0001
Continued use despite social/psychiatric/physical problem	20.6	23.1	0.0008
Marked tolerance	23.1	26.1	0.0007
Withdrawal	24.3	25.9	0.0669
Use to avoid/relieve withdrawal	24.2	26.8	0.0163

KEY: SARA/ERSA=Substance Abuse and Risk for AIDS/Efforts to Reduce the Spread of AIDS

early users and 25.2 years for later users). For all symptoms, the differences between the two groups were statistically significant; for all but two symptoms, withdrawal and withdrawal avoidance, these differences were significant at the 0.01 level.

Psychiatric Comorbidity

The primary focus of this chapter is the comorbidity of psychiatric disorders with substance use and dependence. A substantial proportion of the women in this sample met the criteria for these disorders, as shown in table 5. The most commonly identified disorder in both groups was phobic disorder, followed by depression, ASPD, and PTSD. Women who were early users were more likely than later users to meet the criteria for any one of these diagnoses, except for generalized anxiety and pathological gambling. Of the coexisting diagnoses found to be statistically significant, ASPD and depression had the most significant difference in rates of occurrence between the two groups (ASPD=30 percent early v. 15 percent later, p=0.001; depression=33 percent early v. 15 percent later, p=0.001).

ASPD and Depression

The next analysis describes the lifetime co-occurrence of ASPD and depression. As shown in figure 1, early users were more likely than later users to have histories of comorbid ASPD and depression (10 percent v.

TABLE 5. *Psychiatric comorbidity among SARA/ERSA drug-using women (percent)*

Disorder	Early Users (N=187)	Later Users (N=151)	p
Phobia	45	32	0.014
Panic	6	1	0.049
Generalized anxiety	8	6	NS
Posttraumatic stress disorder*	20	8	0.052
Major depression	33	15	0.001
Antisocial personality disorder	30	15	0.001
Pathological gambling	3	3	NS

*Among ERSA subjects only

KEY: SARA/ERSA=Substance Abuse and Risk for AIDS/Efforts to Reduce the Spread of AIDS; NS=not significant
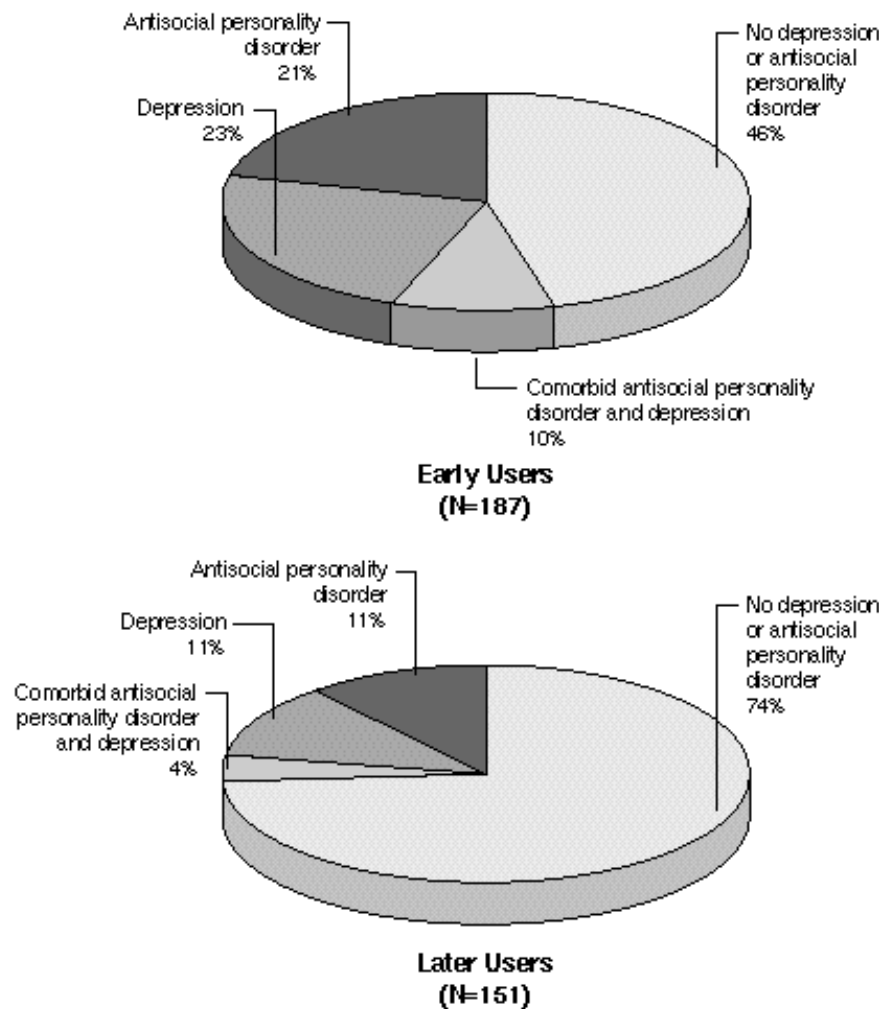
FIGURE 1. *Comorbidity of antisocial personality disorder and depression among SARA/ERSA drug-using women*

KEY: SARA/ERSA=Substance Abuse and Risk for AIDS/Efforts to Reduce the Spread of AIDS

4 percent). Early users were also more likely to have higher rates of each diagnosis separately (depression=23 percent v. 11 percent; ASPD= 21 percent v. 11 percent).

With regard to the most severe symptoms of depression, a large proportion of these women reported thoughts of death, wanting to die, thoughts of suicide, and attempting suicide (table 6), indicating a

TABLE 6. *Characteristics of depression among SARA/ERSA drug-using women (percent)*

Characteristic	Early Users (N=187)	Later Users (N=151)
Thoughts of death	55	46
Felt like dying	42	36
Thoughts of suicide	50	42
Attempted suicide	34	28

KEY: SARA/ERSA=Substance Abuse and Risk for AIDS/Efforts to Reduce the Spread of AIDS

severity of illness that is of considerable concern. Although these high rates did not differ significantly between the groups, early users were more likely to report each of these symptoms. Differences between the two groups in specified adult antisocial behaviors are shown in table 7. The most commonly reported behaviors among the early users were failure to conform to social norms, irritability and aggressivity, and inability to sustain consistent work behavior. Three behaviors discriminated between the two groups: irritability and aggressivity, recklessness regarding one's own or another's safety, and lack of remorse.

TABLE 7. *Specific* DSM-III-R *antisocial personality symptoms among SARA/ERSA drug-using women (percent)*

Symptoms	Early Users (N=187)	Later Users (N=151)
Inability to sustain consistent work behavior	71	72
Failure to conform to social norms of legal behavior	89	83
Irritable and aggressive behavior	74	63*
Repeated failure to honor financial obligations	43	38
Failure to plan ahead or impulsive behavior	37	39
No regard for truth	53	50
Recklessness regarding one's own or another's personal safety	36	26†
Inability to function as a responsible parent or guardian	30	34
Failure to sustain a monogamous relationship	10	7
Lack of remorse for hurting or stealing	42	23†

*0.01<p 0.05, relative to Early Users group
†p=0.001, relative to Early Users group

KEY: *DSM-III-R=Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised;* SARA/ERSA=Substance Abuse and Risk for AIDS/Efforts to Reduce the Spread of AIDS

To understand more about the relationship between early drug use and comorbid ASPD and depression, the authors evaluated the age of onset of these two disorders in relation to the age of onset of drug use and found that ASPD and depression were temporally subsequent to first use of any drug. As shown in table 8, on average, drug use among the early users preceded adult antisocial behavior by 1.6 years, whereas the later users seemed to meet criteria for ASPD at the same time as their drug use initiation. Onset of depression, on the other hand, was reported from more than 3 to more than 5 years after the initiation of drug use, indicating that drug use is a strong risk factor for depression in both groups.

DISCUSSION

The authors studied the early and later onset of drug use in a sample of both in-treatment and out-of-treatment female drug users and found that the use of virtually all substances was more prevalent among early users than among later users. In fact, for almost all drugs, the rates of drug use among early users were more than double those of the later users. However, except for alcohol, the greater rates of use were not associated with a difference in rates of dependence between the two groups. Furthermore, women categorized as early users were more likely to have experienced consequences of any drug from 2 to 4 years earlier than women categorized as later users.

Except for generalized anxiety and pathological gambling, early users were more likely than later users to meet the criteria for any given one of the diagnoses. Of those diagnoses assessed and found to be statistically significant, ASPD and depression varied the most between the two groups. These findings are unique in that they focus on the

TABLE 8. *Age of onset of depression or antisocial personality disorder in relation to drug use*

| | Mean Age at Onset | | |
Disorder	Early Users (N=187)	Later Users (N=151)	p
Depression	20.7	24.5	0.006
Adult antisocial behaviors	17.6	18.9	0.013
Drug use	16.0	18.7	0.001

presence of these two disorders. Early users were more likely than later users to have histories of comorbid ASPD and depression. They were also more likely to have higher rates of each diagnosis separately. In fact, a large proportion of this sample, regardless of age of onset of substance use, indicated an intensity of depressive illness that in itself is of considerable concern. In addition, women who began to use drugs earlier were more likely to be irritable and aggressive, reckless regarding their own or another's safety, and lacking remorse for their behavior.

Finally, early users were found to have ASPD sequelae to drug use. Later users met the criteria for ASPD shortly after drug use initiation, suggesting that their ASPD behaviors might have led them to use drugs or that their drug use was just beginning to cause antisocial behaviors. Drug use was a strong risk factor for depression in both the early and later use groups.

These findings may be limited by the nature of comorbidity research in general, where multiple conditions must be considered. There are issues regarding the assessment, recall, hierarchies of diagnoses, misclassification bias, and nosologies that might complicate interpretation of these results. For example, although it might be argued that data collected by nonclinicians might be less valid than data collected by clinicians, this study minimized this risk by using well-trained nonclinicians who demonstrated a high level of expertise. Comorbidity research might also be limited by the possibility of selective recall bias. If there were selective recall for events, it could affect recall of either psychiatric symptoms or substance use. In this study, any recall bias probably affected measures for both psychiatric symptoms and substance use in the same direction for early and later users, because early users also reported early onset of psychiatric symptoms and later users reported later onset of psychiatric symptoms. Also, because neither study focused on determining the association between early and later onset of use, the respondents and interviewers could not have known of this post-data-collection hypothesis.

Arguments against a misclassification bias include the compatibility of these results with those of Brooner and colleagues (1997). With the identical number of women in the authors' studies (n=338)—a coincidence—the authors found the prevalence of psychiatric disorders, as assessed with a different structured interview, to be comparable, especially for depression and ASPD.

CONCLUSION

These findings, which are generalizable to female drug abusers both in and out of treatment, indicate that women who begin to use drugs at later ages are not much better off than women who begin to use drugs at earlier ages. The later users showed psychiatric profiles that were similar to those of the early users—who themselves showed considerable signs of impairment. These findings suggest that starting drug use at a later age does not reduce the harm of drugs; it only delays its onset. Once drugs are used, the symptoms are not far behind.

These findings, which emphasize that early drug users experience problems from drugs earlier in their lives than later drug users, should influence policy decisions regarding the availability of early treatment and intervention for women who use drugs. They should also highlight the need for special treatment focusing on the comorbid conditions of depression and antisocial behaviors among female substance abusers.

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