

**The Cedar Project: Prevalence of hepatitis C virus infection and related vulnerabilities among young Aboriginal people who use drugs in Two Canadian Cities**

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## ABSTRACT

**Background:** This study sought to estimate the prevalence and incidence of hepatitis C virus (HCV) infection and to identify risk factors associated with HCV infection among Aboriginal young people who use injection and non-injection drugs.

**Methods:** The Cedar Project is a longitudinal study of Aboriginal young people living in Vancouver and Prince George, British Columbia. Eligibility criteria include age between 14 and 30, and self-reported use of non-injection or injection drugs at least once in the month before enrolment. At each visit, participants complete a detailed questionnaire administered by an Aboriginal interviewer. This analysis was based on 512 young people that were recruited between September 2003 and April 2005.

**Results:** Among all members of our cohort, HCV prevalence was 34.8% [95%CI: 30.6-38.9] with similar rates in Prince George and Vancouver (34.5% vs. 35.0%;  $p=0.369$ ). Among those who injected drugs (IDU) at baseline ( $n=286$ ), HCV prevalence was 59.4% [95% CI: 53.8-65.1]. Prevalence was slightly higher among young Aboriginal participants who use injection drugs in Prince George than Vancouver (62.4% vs. 57.1%;  $p=0.369$ ). HCV prevalence among participants who do not use injection drugs ( $n=226$ ) was 3.5%. In multivariable analysis, risk factors that were significantly associated with HCV prevalence among injection drug users included: duration of injection drug use (per year) [AOR=1.4, 95%CI: 1.3-1.5], daily injection of opiates [AOR=2.7, 95%CI: 1.0-7.4], reusing rigs [AOR=2.4, 95%CI: 1.3-4.4], female gender [AOR=1.9, 95%CI: 1.1-3.4], and having one or more parents that attended residential school [AOR=1.9, 95%CI: 1.1-3.4].

**Conclusions:** HCV prevalence and incidence rates are elevated among Aboriginal young people who use drugs and reside in Vancouver and Prince George. Culturally based prevention, treatment, and harm reduction programs are urgently needed in this population.

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## INTRODUCTION

Aboriginal scholars have long suggested that any discussions related to addictions and concomitant vulnerability to infectious disease must be framed within the context of the historical legacy of colonization, including forced removal from traditional lands, cultural genocide and, in particular, the history of the residential school system. Yet, little is known about the extent of the hepatitis C (HCV) epidemic among Aboriginal people in North America [1, 2]. In Canada, the reasons for this include limited HCV surveillance data, underreporting and inconsistent ethnicity documentation between the provinces [3]. Therefore national surveillance data can offer only a minimum estimate of the number of infected persons. Regrettably, indicated by the few studies that are available, alarming trends have already emerged. The Public Health Agency of Canada estimates that HCV prevalence among Aboriginal people in Canada is seven-fold higher than among non-Aboriginal people. This compares to an estimated prevalence of 0.8 percent among the general population [3]. Estimates also suggest that the numbers of new cases of HCV are eight times higher among Aboriginal people than in the general population. These data, however, represent Aboriginal people who live in urban areas and may not be generalizable to the entire Aboriginal population. A recent analysis conducted by First Nations and Inuit Health Branch, found that Status Indians represented 4 percent of the population of the province of British Columbia but accounted for 10 percent of hepatitis C infections reported in 2001 [4]. Other data indicate HCV prevalence among Aboriginal populations in different regions of Canada range between 0.4 to 29.3 percent [1].

More than 80 percent of the injection drug using population in Vancouver is infected with HCV [5]. Prevalence rates among Aboriginal people who use injection drugs have been estimated to be over 90 percent [5] and the virus is contracted early on in the injection career of

people who use drugs. [6, 7, 8]. A recent study in Vancouver found an astonishing incidence rate of 37.3 per 100-person years among young people who use drugs [9]. At a time when indigenous people's vulnerability to HCV infection and other infectious diseases is becoming increasingly apparent worldwide, a better understanding of the factors and processes that cause drug related harm among Aboriginal young people is urgently required. Whereas some factors unique to the transmission of infectious disease among young people in Canada who use injection drugs are known, basic and behavioral research efforts addressing sex related and drug related vulnerabilities among young Aboriginal people who use drugs are lacking; particularly in smaller city centers and in reserve communities [10].

The primary objective of this investigation was to estimate the prevalence rate of HCV infection among young Aboriginal people who use drugs and reside in Vancouver and Prince George. In addition, we sought to identify demographic and behavioural factors associated with HCV prevalence in this population.

## METHODS

Guidelines provided in the Canadian Tri-Council Policy Statement: Ethical Conduct for Research Involving Human Subjects were followed in the development and conduct of this study, with particular attention to section 6.0 pertaining to research involving Aboriginal subjects. Our First Nation's collaborators, including Aboriginal AIDS Service Organizations, were involved in the conception, design and implementation of the Cedar Project. They also reviewed the results of this analysis and approved this manuscript for publication. The study was also approved by the University of British Columbia/Providence Health Care Research Ethics Board.

The Cedar study is an ongoing prospective cohort study of young Aboriginal people who use drugs in Vancouver and Prince George with target recruitments of 300 subjects in each city. Eligibility criteria stipulate that participants must be between 14 and 30 years of age, and smoked or injected illicit drugs including crystal methamphetamine, crack-cocaine, heroin or cocaine in the month prior to enrolment. Participants were eligible to participate if they had been residing in the greater Vancouver or Prince George Regions respectively, and have provided written informed consent. Participants in both cities were recruited through referral by health care providers, community outreach, and by word of mouth. Based on 2001 Census data, there are estimated to be 26,890 young Aboriginal people between the ages of 15 and 34 residing in the Northern Health Authority and 11,450 in the Vancouver Coastal Health Authority. The latter authorities contain Prince George and Vancouver respectively.

All participants met with one study coordinator who explained procedures, sought informed consent and confirmed study eligibility. Venous blood samples were drawn and tested for HIV and Hepatitis C antibodies and interviewers were blinded to the HIV and Hepatitis C status of the subjects. At enrolment, participants completed an interviewer-administered questionnaire to elicit socio-demographic data and data on non-injection and injection drug use, injection practices, sexual risk behaviours and service utilization. Aboriginal study personnel conducted the interviews. We used testing algorithms similar to other studies conducted in this region. In brief, AxSYM HCV version 3.0 (Abbott Laboratories, Chicago IL) was used to screen all plasma samples. Negative samples did not undergo further testing. All positive samples underwent further testing with recombinant ORTHO HCV 3.0 ELISA test system (Ortho-Clinical Diagnostic Inc, Rochester NY). Samples that tested positive in both assays were classified as positive. Samples that tested positive by AxSYM HCV, negative by Ortho HCV were classified as

negative. All eligible participants had private interviews including pre and post-test counseling with trained nurses; participants were requested to return for their HCV sero-status test result at which time referral for HIV/AIDS and hepatitis C care was provided. In addition, subjects were also referred to clinics that provide immunization against hepatitis A and B. Participants were given a small stipend at each study visit as compensation for their time and to facilitate transportation.

To estimate HCV prevalence we identified 512 participants who were recruited between September 2003 and April 2005, had completed their baseline interview, and had had an HCV antibody test. To estimate HCV incidence, we identified 198 participants who completed their enrolment visit between September 2003 and October 2004, were HCV-negative at enrolment, and completed at least one follow-up visit during the observation period (September 2003 to April 2005). The event of interest in this analysis was 'HCV infection'. For HCV seroincident participants, time to HCV infection was calculated as the duration (in months) between the date of the first positive antibody test result and the date of enrolment. Follow-up time for event-free participants was calculated as the duration between the date of their most recent negative antibody test result and their date of enrolment. Estimates of HCV incidence were determined using crude rates and incidence density methods. To assess the strength of association between factors of interest and HCV infection, we calculated both unadjusted and adjusted odds ratios and 95 percent confidence intervals. The low number of HCV seroconversions (n=21) at this time did not allow a thorough analysis of risk factors for incident infection.

Because of the known association of these viruses with parenteral drug use, HCV prevalence rates were stratified by injection and non-injection drug use, and risk factor analyses were restricted to those reporting injection of drugs. Variables of interest included age, income,

incarceration and stable versus unstable housing. Participants who reported having stable housing were those living in their own house or apartment. Unstable housing was defined as living arrangements that included single room occupancy hotels (SROs), transitional living arrangements ('couch surfing'), and homelessness. Risky injection variables included borrowing and lending syringes that had been used by someone else. Drug use behaviors included frequent injection, type of drug, bingeing behavior and overdose experience. As in previous reports, we defined frequent cocaine, heroin and speedball users as those who reported injecting cocaine, heroin or speedballs (cocaine and heroin) once or more per day respectively. Bingeing was defined as periods when drugs were injected more frequently than usual. Risk factors regarding sexual behavior included having an HCV positive sexual partner in the last six months and exchanging money or drugs for sex in the last six months.

Statistical analyses of bivariable categorical data were conducted using Pearson's chi-squared test. Fisher's exact test was used to analyze bivariable categorical data when 25 percent or more of the expected cell frequencies in a contingency table were less than five. Comparisons of numeric variables (e.g. age at enrolment, age at first injection) between participants residing in Vancouver and Prince George were conducted using Wilcoxon's rank-sum test. Multivariable logistic regression analysis was used to model the independent association of demographic variables and behavioural risk factors with HCV infection. Unadjusted odds ratios and 95 percent confidence intervals were obtained using logistic regression. All reported p-values are two-sided.

## RESULTS

Demographic characteristics of Cedar Project participants are summarized in Table 1. Among 512 participants that completed HCV antibody testing at enrolment, 178 were positive (34.5%) yielding a prevalence of 34.8%. HCV prevalence was similar in Vancouver and Prince George (35.0% vs. 34.5%). Among baseline participants who use injection drugs (n=286), 170 tested positive and HCV prevalence was 59.4%. HCV prevalence was higher among participants who use injection drugs in Prince George than Vancouver (62.4% vs. 57.1%) but this difference was not statistically significant. HCV prevalence among participants who did not use injection drugs (n=226) was 3.5%. We followed 198 participants that were HCV negative at enrolment for a median of 11 months. These participants contributed 213 person years of observation (data not shown). During the observation period, 21 new infections were recorded in this cohort. This yielded a crude incidence rate of 10.6% and an incidence density estimate of 12.7 per 100 person years (PY). HCV incidence was higher in Prince George than in Vancouver (15.9 vs. 10.0 per 100 PY) but this difference was not statistically significant. Among HCV-negative participants that reported injection drug use at the enrolment visit (n=71), the incidence density was 22.6 per 100 PY. Among participants who did not use injection drugs (at enrolment), this rate was 6.7 per 100 PY. Fourteen of the twenty-one seroconverters (67%) reported using injection drugs at enrolment but seven (33%) did not. The remaining seven participants all reported using injection drugs at one or more of their follow-up visits.

Among participants who use injection drugs in the cohort, HCV prevalence was significantly associated with daily injection of speedballs, morphine, cocaine, dilaudid, and heroin. As shown in Table 2, in unadjusted analyses, HCV prevalence was positively associated with current or past methadone treatment, involvement in the sex trade, female gender,



incarceration, having one or both parents that attended residential school, and reusing rigs. We also investigated the association of duration of smoking and injecting drugs with HCV prevalence (Table 3). Duration of injecting and smoking drugs as well as age were strong predictors of HCV prevalence in unadjusted analyses. HCV positive participants reported significantly longer periods of smoking and injecting drugs compared to HCV negative participants. HCV positive participants were also older at enrolment than their HCV negative counterparts.

Demographic and behavioural variables that were at least marginally significant in unadjusted analyses ( $p < 0.10$ ) were considered for inclusion in a multivariable logistic regression model. Because the numbers of HCV positive and negative participants that reported daily use of some opiates were small, for the purpose of multivariable analysis we combined these variables into a single variable. This composite variable was defined as daily injection of one or more of the following opiates: speedballs, morphine, or dilaudid. In multivariable analysis (Table 4), risk factors that were independently associated with HCV prevalence included: duration of injection drug use, daily injection of opiates, reusing rigs, female gender, and having one or more parents that attended residential school. Estimates of risk for the variables in this multivariable model were similar after adjustment for geographic location.

## **INTERPRETATION**

To our knowledge, this is the first epidemiological study in Canada to monitor HCV prevalence and associated risk factors among young Aboriginal people who use drugs. In addition, no other epidemiological studies have reported a statistical association between vulnerability to infectious disease and the legacy of the residential school system. The spread of HCV to levels above 60% in this group of young people who use injection drugs in both cities was an unexpected finding and reflects how rapidly this virus can spread even in the early period just after injection begins [8]. At baseline, 38% of the HCV positive young people reported that they had been injecting drugs for two years or less. The fact that prevalence of HCV among young Aboriginal people who use injection drugs in our study (59%) was higher than the prevalence in young people who use drugs reported in Vancouver (46%) is of concern [9]. Given that Vancouver has consistently been described as an epicenter of the HIV and HCV epidemics in British Columbia and in Canada since the early 1980's, these findings indicate that the faces of these epidemics are changing. The fact that HCV infection among young people who use drugs in this northern community mirrored those of the DTES is of grave concern. Based on the estimates we have obtained in this study, we speculate similar rates of HCV infection will be observed in smaller, northern communities throughout British Columbia.

We found duration of injection, frequent injection of opiates and reusing previously used syringes, to be independently associated with baseline HCV positivity. The strong association between frequent opiate use and HCV prevalence is a relatively new finding in this setting. A persistent risk factor for blood borne infection in Vancouver's downtown eastside is the frequent use of injection cocaine [11, 12]. The fact that young people are injecting a wide array of opiates, morphine, dilaudid and speedballs, along with cocaine on a daily basis and that daily

opiate use and not cocaine use was associated with HCV seropositivity warrants further investigation. Methadone maintenance therapy (MMT) appeared to be associated with HCV infection in bivariate analyses. It is important to note, however, that participants reporting past or current MMT were older than those not so reporting so that the association of MMT with HCV is confounded by age. Methadone maintenance therapy (MMT) is the primary treatment modality for opiate addiction in Canada and has proven to be effective at preventing HIV infection [13]. Methadone maintenance therapy (MMT) appeared to be associated with HCV infection in bivariate analyses. It is important to note, however, that participants reporting past or current MMT were older than those not so reporting so that the association of MMT with HCV is confounded by age. Unfortunately, the evidence supporting effectiveness in reducing HCV incidence is less substantial [14, 15]. Despite this lack of evidence, treatment providers continue to recommend MMT because it is more likely that injection episodes are safer when they occur, because as an opioid replacement therapy, it helps reduce the number of daily injections. Increased efforts must be made to determine the barriers to receiving such treatment for Aboriginal young people, particularly in smaller city centres.

We found that reusing rigs was another significant risk factor for HCV infection in our study. Because of previously demonstrated associations between other high-risk behaviors related to accessibility of clean syringes [16] we compared, participants who used injection drugs in our cohort and reported reusing their rig during the six months before enrolment with those who did not. Indeed, participants that reported reusing their syringes were significantly more likely to report borrowing and sharing syringes, bingeing with injection drugs, and requiring assistance injecting during the past six months. Not surprisingly, 're-using rig' was more prevalent among participants who use injection drugs in Prince George (46%), the northern

community compared to Vancouver (24%), a city with well supported needle distribution programmes.

Female gender was significantly associated with HCV infection even after adjustment for demographic and behavioural risk factors. While the majority of these infections can be attributed to injection related risks, it is important to highlight that many young Aboriginal women are intimately involved with men who are usually older and who use injection drugs themselves [17, 18]. Indeed research has demonstrated that for women who rely on their partners for drug acquisition, preparation and injection, the distribution of power and control in sexual and injection relationships often lies with drug injecting men who control the money and the drugs [19, 20]. Combined, these factors lead to a greater likelihood of unsafe sex and to the female partner more likely being “second on the needle.” We found no evidence that HCV was transmitted sexually. In other studies involving young people who use drugs, participants have reported high rates of childhood sexual victimization and sex work related violence [19]. However, many girls in this study are involved in survival sex work and yet few services aimed at reducing drug or sex related harm for these young women exist, particularly in the North. Any efforts to help alleviate the impact of drug related harm in both rural and urban settings must be inclusive of the perspectives of young men and young women and they must be afforded the opportunity to provide leadership in the decisions made about programming that reflects their needs [20]. In addition, when designing new programming service providers must remain mindful of how the past can shape the response to prevention initiatives, including histories of mistrust, toward both regional and federal authorities [21, 22].

In recent years the Government of Canada and Aboriginal communities all across the country have been debating the relative toll of the cumulative and intergenerational effects of

historical trauma related to the Indian Residential School System [23]. Legislated by the Gradual Civilization Act in 1857 many researchers have concluded, based upon testimony given by family and community that the forced removal of children from their homes and placement in boarding schools, is directly responsible for poor health outcomes of survivors, including the abuse of drugs and alcohol [24]. Currently, there are an estimated 80,000 living survivors of the residential school system in Canada, of whom 35,000 live in British Columbia [25]. As former students raise their children and grandchildren, the intergenerational effects of abuse and familial fragmentation become evident [26, 27]. Several Aboriginal AIDS service providers have suggested drug use is just one way that people deal with the complex effects of poverty, despair, discrimination, loss of language and traditional territories and the erosion of culture [28]. Residential School survivors themselves have testified that the legacy of the residential school system is multigenerational and that their own children, who themselves never attended the schools are also heavily impacted by familial stress and despair. Previous research has identified univariable relationships between having a parent who attended residential school and involvement in the child welfare system with sexual abuse among young Aboriginal people who use drugs in British Columbia [29]. To our knowledge, no other epidemiological studies have reported a statistical association between vulnerability to infectious disease and the legacy of the residential school system. The mechanism of effect between residential school attendance by parents and higher risk for hepatitis C positivity should be the subject of further study. As indigenous scholars have noted, many First Nations families continue to express their ceremonial rites and obligations despite over 500 years of missionary activities and colonial suppression [30, 31]. In order to develop early community-based responses to the sexual and drug-related vulnerabilities faced by Aboriginal young people, participatory research and programming

processes that address the importance of ceremonial and familial obligations related to the safety of Aboriginal children and young people must be prioritized [32].

Several limitations of this study should be acknowledged. This study is based on self-reported behavioural data obtained from a non-probability sample of individuals. Consequently, there is potential for recall bias, socially desirable reporting, and misclassification of exposure variables in this study. Responses to questions concerning drug use and sexual behaviors may be influenced by the participant's knowledge of their HCV antibody status. In addition, recall problems may exist with reporting of past traumatic life events (e.g. being taken from biological parents, whether parents attended residential school, and sexual abuse or non-consensual sex). The effect of memory on our estimates of risk for these factors is difficult to assess. Non-differential misclassification of an exposure variable and the resultant bias can lead to a relative risk estimate that may be either toward or away from the null hypothesis [33]. Despite these limitations, we believe these data provide important epidemiological information about a high-risk Aboriginal population that has not been previously studied.

In the absence of post-exposure prophylaxis for HCV and an effective vaccine for HCV, primary prevention programs must focus on safe injection practices and reducing the number of people who initiate injection drug use. Such high baseline prevalence rates underscore the importance of carefully examining the effectiveness of current harm reduction initiatives in both rural and urban settings and suggest that scaling up successful initiatives for the reduction of escalating incidence must be an urgent priority. Culturally safe prevention, treatment, and harm reduction programs are urgently required in this population. With significant increases in resources, acknowledging the intergenerational trauma related to the residential school system

may be one way that Aboriginal leadership and addiction specialists and other practitioners can begin to mitigate the potential impact of the epidemic currently threatening their communities.

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**Conflict of Interest Statement:** We declare that we have no conflict of interest

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Table 1: Demographic characteristics of 512 Cedar Project participants

Variable	n (%)
Female gender	265 (52)
Age at enrolment visit	<u>Years</u>
Median	23
Range	14 to 30
Straight Social/Sexual Identity	456 (89)
Single marital status	390 (76)
Did not complete high school	423 (83)
Unstable housing	230 (45)
Had one or more parent attend residential school	286 (56)
Taken from biological parents (ever)	327 (64)
Age first taken from biological parents	<u>Years</u>
Median	5
Range	1 to 19
Nonconsensual sex (ever)	244 (48)
Age first nonconsensual sex	<u>Years</u>
Median	7
Range	1 to 25
Attempted suicide (ever)	187 (37)
Incarcerated (ever)	342 (67)
Age first incarcerated	<u>Years</u>
Median	16
Range	10 to 28
Ever been pregnant (females only)	201 (39)
Involvement in survival sex work (ever)	195 (38)
Age of first involvement in survival sex work	<u>Years</u>
Median	16
Range	10 to 28
Injection drug use	286 (56)



Table 2: Comparison of risk factors (including unadjusted odds ratios) between HCV positive and HCV negative Aboriginal young people that use injection drugs

Variable	HCV-positive %	HCV – negative %	p-value	Odds Ratio	95% CI
Speedballs (one or more injections per day)	13.0	2.6	0.002	5.6	1.6, 19.3
Ever been in a methadone treatment program	35.9	12.1	<0.001	4.1	2.1, 7.7
Morphine (one or more injections per day)	8.8	2.6	0.033	3.7	1.0, 12.9
Currently in a methadone treatment program	14.1	4.3	0.007	3.6	1.4, 9.9
Cocaine (one or more injections per day)	36.5	14.7	<0.001	3.3	1.8, 6.1
Dilaudid (one or more injections per day)	7.6	2.6	0.068	3.1	0.9, 11.2
Reusing own rig	41.2	21.5	<0.001	2.5	1.5, 4.4
Sex with client in previous six months	44.7	26.7	0.002	2.2	1.3, 3.7
Paid for sex (ever)	57.1	39.7	0.004	2.0	1.3, 3.3
Heroin (one or more injections per day)	32.9	19.8	0.015	2.0	1.1, 3.5
Gender (female)	62.4	47.4	0.012	1.9	1.1, 3.0
Ever been in a prison/jail/detention centre overnight	81.2	69.8	0.026	1.9	1.1, 3.2
Parents attended residential school	62.4	50.0	0.038	1.7	1.0, 2.7
Ever been in an alcohol or other drug treatment program	80.6	71.6	0.075	1.7	0.9, 2.8
Borrowing injection equipment	20.0	12.9	0.119	1.7	0.9, 3.3
Difficulty accessing clean needles	15.5	11.1	0.355	1.5	0.6, 3.4
Detained by police	83.5	78.5	0.278	1.4	0.8, 2.5
Bingeing or runs	20.0	16.4	0.439	1.3	0.7, 2.4
Location (Prince George)	45.9	40.5	0.369	1.2	0.8, 2.0
Completed high school, or attended technical school, college or university	19.1	16.5	0.587	1.2	0.6, 2.2
Non-consensual sex (ever)	54.1	54.3	0.974	1.0	0.6, 1.6
Taken from biological parents	62.4	63.8	0.804	0.9	0.6, 1.5
Unstable housing	51.9	57.7	0.344	0.8	0.5, 1.2
Attempted suicide	37.7	43.1	0.355	0.8	0.5, 1.3
Crystal meth (one or more injections per day)	6.1	7.6	0.655	0.8	0.3, 2.1
Require help injecting	27.1	36.2	0.100	0.7	0.4, 1.1

Table 3: Comparison of duration of drug use and age at enrolment (including unadjusted odds ratios) between HCV positive and HCV negative Aboriginal young people that use injection drugs

Variable	HCV-positive	HCV – negative	p-value	Odds Ratio	95% CI
Duration of injection drug use (years)	5 <1 -15	1 <1 - 10	<0.001	1.42	1.26, 1.56
Duration smoking drugs (years)	7 <1 -17	4 <1 -15	<0.001	1.12	1.05, 1.20
Age (years)	25	24	0.004	1.11	1.03, 1.18

	14 - 30	15 - 30			
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Table 4: Multivariable logistic regression model of risk factors associated with HCV infection among 286 Aboriginal young people that use injection drugs

<b>Variable</b>	<b>Adjusted Odds Ratio</b>	<b>95% CI</b>
Daily injection of opiates (speedballs, morphine, or dilaudid)	2.7	1.0, 7.4
Reusing own rig	2.4	1.3, 4.4
Female gender	1.9	1.1, 3.4
One or both parents attended residential school	1.9	1.1, 3.4
Duration of injection drug use (per year)	1.4	1.3, 1.5

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