Public Health and Hepatitis C

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This paper reviews key public health aspects related to surveillance, transmission and primary prevention of hepatitis C. Hepatitis C is now a reportable disease in all Canadian provinces and territories. Although prevalence in Canada is estimated at under 1%, that associated with injection drug use (IDU) approaches 90%. The epidemiology of new HCV infections in Canada is now primarily defined by IDU behaviour, with annual incidence rates among new drug injectors exceeding 25%. HCV is less efficiently transmitted through other routes of exposure. An effective vaccine against HCV remains elusive. Some jurisdictions offer hepatitis A and hepatitis B vaccine to HCV-infected persons. An array of harm reduction strategies targeting IDU has been implemented but underdeployed across Canada, and has been ineffective to date in controlling the HCV epidemic. Public policy alternatives, such as legalization and regulation of injection drugs, are being debated. Improved HCV preventive strategies are urgently required and need careful evaluation.

Public health practitioners carry responsibility for the surveillance and primary prevention of Hepatitis C Virus (HCV) infection. This paper will review key aspects relevant to all disciplines concerned with public health in the areas of surveillance, transmission and primary prevention.

SURVEILLANCE

A co-ordinated surveillance approach is necessary to determine disease incidence, risk factors and transmission patterns for HCV infection. A well-tooled system will assist in evaluating existing programs and identifying issues where further action is needed.

The 1998 Health Canada HCV consensus conference recommended that three different surveillance approaches should be taken: case-by-case surveillance, enhanced surveillance in sentinel health units, and enhanced surveillance targeting specific locations or populations.[1] National reporting of HCV in Canada began in 1992, but the infection has only been reportable in all provinces and territories since January 1, 1999. In 1998 LCDC established a project of enhanced surveillance for newly identified HCV infections, collecting detailed information from physicians and patient interviews. The project is being expanded beyond the current 4 sites to include other urban and rural areas. Surveillance of acute symptomatic HCV infection can provide a means to evaluate the effectiveness of prevention efforts and to identify missed opportunities for prevention.[2]

The number of cases of HCV reported in Canada has dramatically increased from 1,321 in 1992 to 21,885 in 1998 (final number for 1999 is not yet available),[3] mainly due to an increased recognition of previously acquired HCV infection. Prevalence in the general Canadian population has been estimated at 0.8% (240,000 people currently infected).[4] A similar prevalence of 1% was found in pregnant women in British Columbia[2] and also at a community-based electroencephalogram clinic in Ontario.[5]

TRANSMISSION

Although HCV ribonucleic acid (RNA) has been detected in a wide range of body fluids and tissues (e.g., saliva, tears, breastmilk, vaginal secretions, seminal fluid), transmission is correlated primarily with exposure to blood.[6-8] Serum HCV-RNA titres of 10^6 copies per millilitre or more, measured by reverse transcriptase polymerase chain reaction, are more commonly associated with HCV transmission, but a specific threshold of viral load predicting infection cannot be defined.[9,10] Transmission is also driven by the high proportion of HCV-infected persons – approximately 85% – who develop chronic infection. Transmission risk for HCV following a single percutaneous exposure is intermediate (2.7-6%), compared to risk of HIV (0.3%) and hepatitis B virus (19-30% in HBeAg-positive source).[11]

Injection drug use

The majority of new HCV infections in Canada, as well as approximately 70% of prevalent infections, occur among injecting drug users (IDUs).[12] The high prevalence of chronic HCV in IDU populations, along with highly efficient transmission associated with the sharing of syringes and other paraphernalia, and a steady influx of new, susceptible injecting users have resulted in sustained high incidence rates among IDU populations, even with infrequent sharing of needles and syringes.[13] Among IDU cohorts in Vancouver and Montreal, the prevalence of HCV is reported as 87% and 70% respectively, and the annual incidence is reported as 26% and 27% respectively.[1,14,15] A dramatic increase in prevalence of HCV within the first 2 years of injecting drug use was found in the US-based ALIVE study. Thus prevention measures should target new injection drug users.[16] Recent disclosure of the world's largest known medically caused outbreak of HCV illustrates the remarkable efficiency by which used, non-disinfected needles and other injecting drug

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paraphernalia can transmit HCV. This outbreak involved an anti-schistosomiasis campaign conducted in Egypt from the 1950s to 1980s, in which thousands of persons were administered repeated injections of an antimony salt with re-used needles.[17]

Therapeutic blood and blood products

Blood transfusion, which accounted for a substantial proportion of HCV infections acquired over 10 years ago, now rarely accounts for recently acquired infections.[18] Transmission of HCV from therapeutic blood or blood products has plummeted since 1990, when donor screening was introduced in Canada. An estimated 10-15% of cumulative HCV infections in Canada may have been acquired in this manner.[1] Viral inactivation procedures introduced for clotting factor concentrates and human immune globulins prepared from pooled plasma, have eliminated transmission risk via these products. Third generation anti-HCV screening of all donor blood, introduced in Canada in 1996, has reduced the risk of HCV exposure from blood to approximately 1 in 120,000 donations.[19] Canadian Blood Services introduced nucleic acid testing for HCV for all blood donors in October 1999 as an investigational screening test (pers. commun. P. Doyle, 2000). Recommendations of Justice Krever are also being implemented in some provinces, such as British Columbia, with development of blood and blood product transfusion registries and tracking mechanisms to facilitate lookbacks (positive donor) and tracebacks (positive recipient).

Mother-to-child (vertical transmission)

Mother-to-child transmission of HCV has been found to occur in about 5% of HCV-infected, HIV-negative pregnant populations.[10,20] Co-infection with HCV and HIV is associated with HCV transmission rates about 3 times greater.[2,10,21-23] There is no definite epidemiologic evidence of mother-to-child HCV transmission from breastfeeding involving asymptomatic, HCV-seropositive, HIV-negative mothers with no detectable serum HCV-RNA.[21,23-25] More limited evidence suggests that asymptomatic, HIV-negative mothers with detectable serum HCV-RNA below 10^5 to 10^6 copies/ml but no detectable HCV-RNA in breastmilk are also at very low risk of transmitting HCV by breastfeeding.[26-28] There are conflicting data on the protective value of elective caesarean section.[22]

Sexual transmission

Despite some estimates that up to 20% of new HCV infections may be due to sexual exposure,[18] the literature reports a wide range of risk of interspousal HCV infection, which is inferred to be due to sexual transmission.[29-35] Alternative risk factors may account for many cases of apparent sexual transmission between sexual partners.[29,36,37] A Japanese study, which controlled for parenteral exposures, estimated the risk of spousal transmission to be less than 1%,[38] and no evidence was found of sexual transmission of HCV to husbands of women with hepatitis C who had received contaminated anti-D immunoglobulin.[39] The risk of infection through sexual intercourse with a carrier has been estimated at 2.5% over 20 years.[1] Some studies show increased prevalence of HCV infection in spouses of infected sexual partners compared to other household relatives or matched spouses of non-infected partners;[30,40] others show a correlation with duration of sexual relationship;[41,42] while still others indicate age to be predictive of interspousal and other interfamilial HCV infection.[29,31,32] The risk of transmission through anal intercourse is unknown, although it is biologically plausible that a higher rate of exchange of small amounts of blood could correlate with a higher risk of transmission.

Transmission to non-sexual close contacts

Transmission of HCV to non-sexual household contacts is very low, with most studies reporting approximately 2-3% prevalence of HCV infection among these contacts.[29-35] Transmission may occur through sharing articles that might be contaminated with blood, e.g., toothbrushes and razors.

Other exposures

There is documented transmission of HCV with tattooing,[43] but ear piercing, acupuncture and electrolysis pose little risk for infection.[44] Prevalence of HCV infection among health care workers is about 1 to 2% – the same as among the general population – and the most important risk factor associated with occupational HCV infection is unintentional needlestick injury.[2]

PREVENTION

Hepatitis A prevention

Patients with chronic hepatitis C, unlike those with chronic hepatitis B, were found to have a substantial risk of fulminant hepatitis and death associated with hepatitis A virus infection (HAV).[45] Hepatitis A vaccine is safe and effective[46] and should be made available free of charge to HCV-positive patients and IDUs. Some jurisdictions, such as British Columbia, also offer hepatitis B vaccination to this population. However the IDU population may not access medical care in the usual manner and targeted programs are necessary to reach this population. The Vancouver/Richmond Health Board initiated such a program in January 2000; teams of nurses immunized 3,000 at-risk persons, offering immunization in their residences, the needle exchange, drop-in centres, medical clinics and other locations in the Downtown Eastside of Vancouver.

Immunoprophylaxis

The obstacles to developing a vaccine for primary prevention seem daunting. HCV has a high rate of mutation during RNA polymerisation. A hyper-variable region of its genome codes for an exposed portion of envelope protein.[47-49] Few changes in the exposed area of envelope lead to functional constraints for the virus so that HCV pays a low cost for its ability to evolve swarms of closely related yet genetically distinct quasispecies in the same host. The net result is a moving immunologic target.[50]

While MHA class 2 alleles, CD4 T cell responses, helper cell phenotype and associated cytokine activity have shown an association with viral clearance,[51-56] most infected people show poor clearance of virus. There is no clearly defined protective response after natural infection. The lack of an *in vitro* or ideal animal model has also limited vaccine development. However in one study, a vaccine composed of envelope glycoprotein protected chimpanzees against low-level intravenous challenge by the homologous strain.[57]

Passive immunization has no proven efficacy for pre- or post-exposure prophylaxis.[58] The systematic exclusion of HCV-positive

people from donor pools will assure that even a theoretical benefit from human immunoglobulin cannot be easily evaluated.

Harm reduction measures

Harm reduction is a strategy that may reduce the transmission of many parenteral pathogens. Needle exchange as well as education on syringe cleaning and lower risk injection practices can reduce the risk of HCV transmission. But the majority of IDUs, even where these limited harm reduction measures are in place, still become infected with hepatitis C.[59-63]

Sexual HCV transmission is best prevented through limiting the number of sexual partners and using male or female condoms for each and every sexual encounter.[64] Condoms unequivocally reduce rates of transmission for other STIs that are more efficiently transmitted sexually, including HIV and genital herpes. These strategies are advisable for all casual relationships, especially if anal intercourse is entertained as there remains uncertainty about specific risk associated with that activity. Monogamous couples should be advised of the risk of transmission and of the above strategies, but it is reasonable to leave a decision about long-term barrier method use within the relationship.

Public policy

Public policy (including harm reduction strategies as currently deployed in Canada) has not been successful in controlling the HCV epidemic. For this infection, any scenario which allows even a slight probability of syringe sharing will provide ample opportunity for transmission.

The use of illegal substances is considered by some to be an alternate lifestyle and a matter of personal choice. The pharmacology and social reality of addiction provide other perspectives on that view. Cocaine, for example, stimulates an area of the brain normally responsible for rewarding an individual for actions that promote survival or self-propagation.[65] The result is a sincere desire to repeat the experience. Yet this drive may compromise rather than complement survival.

Many of the adverse health effects from drug misuse relate to their pharmacology as well as to the practice of injection per se. These include hypertensive and vascular events with stimulants, overdose with many classes of drug, the introduction of microorganisms into the circulation and the loss of an individual's ability to provide for herself or others. These sequelae burden the social welfare and health systems and may put children at risk of neglect or abuse.

Another set of harms relates to the legal prohibition of many of the substances of addiction in our society. Participation in the black market puts users at risk of violent death, contaminated supply and overdose from supplies of varying potency. Property and violent crime conducted by addicts to gain funds for costly drugs represent a drain on the fiscal and social welfare of our society.

Effective primary prevention strategies are needed that intervene where people are at risk of initiating addictive drug use or of moving from non-injecting to injecting use. While not an answer for every currently addicted patient, existing treatment strategies such as methadone maintenance, detoxification and abstinence-based treatment strategies are of proven value and must be more widely funded and deployed.

Solutions to the regulatory aspects of the problem are under-researched and controversial. Well-designed medical trials of alternative substitution and maintenance therapies are warranted to establish whether there can be further improvements over the existing benefits of methadone therapy for some patients. Decriminalizing simple possession could lessen the burden on the court system while allowing a greater focus on treatment. Independent of decriminalization, it may be of value to direct users convicted of minor property crimes through a drug court to treatment facilities rather than to jail.

Outright legalization and regulation (as with tobacco and alcohol) has been proposed as a solution by many health advocates. The proposal is to take currently illegal drugs out of the criminal code and place them under health regulation. Components of such a system might include sale/supply of injection drugs only through a licenced pharmacist, regulations to restrict points of sale similar to those for tobacco and alcohol, single-use needles and syringes with a known dose of sterile drug, prices consistent with a licenced supply (as opposed to a black market) and programs to assist addicts with obtaining and maintaining employment.

However, many practitioners retain misgivings about the scope and consequences of a legalization approach.[66-68] Legalization would indeed make safer drugs more available. But while this may help reduce harm to those currently addicted, it is plausible that the greater legitimacy of substance use could broaden the size of the addicted population. In our desire to change things for the better, we must remain connected to the principle of *primum non parum*.

So, where do we go next? Solutions to the hepatitis C epidemic and other problems resulting from addiction will be solved neither by uncritically espousing alternate solutions nor by accepting the status quo. We must assure that effective programs for which there is existing evidence are fully deployed and that imaginative new approaches are considered urgently, implemented thoughtfully and evaluated fully.

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