A B S T R A C T

*Objective:* To determine: a) population-based hepatitis B seroprevalence rates; and b) associated behavioural risk factors.

*Setting:* A remote northern Ontario town with a cluster of hepatitis B cases.

*Interventions:* Anonymous blood testing linked with risk-factor questionnaires.

*Results:* 635 persons aged 14 to 30 years (51% of the eligible age cohort) donated blood in return for free vaccination; four were anti-HBs positive, and none was HBsAg positive. In all, 19% of participants reported two or more sexual partners in the previous year, 6% reported at least one tattooing in the previous year, and 1% reported illicit injection drug use. Of persons with multiple sexual partners 84% did not consistently use condoms.

*Conclusions:* When the serological results of the original cluster (and contacts) were considered, the age cohort's HBsAg seroprevalence rate was estimated to be between 0.24% and 0.47%. While the serosurvey did not discover additional HBsAg positive cases, there was great potential for heterosexual transmission.

# A B R É G É

*Objectif :* Déterminer a) la séroprévalence de l'hépatite B chez une population et b) les facteurs de risque associés au comportement.

*Cadre :* Une ville éloignée du nord de l'Ontario où s'est récemment manifestée une poussée d'infections par le virus de l'hépatite B.

*Interventions :* Analyses de sang anonymes et questionnaires sur les facteurs de risque.

Résultats : Six cent trente-cinq personnes entre les âges de 14 et 30 ans ont donné un prélèvement de sang (51 % des personnes dans le groupe d'âge étudié) et ont accepté de se faire vacciner gratuitement contre l'hépatite B. Quatre personnes ont eu des résultats positifs à l'égard de l'anticorps anti-HBs et aucune n'a eu des résultats positifs à l'égard de l'HBsAg. Parmi les personnes ayant rempli le questionnaire, 19 % ont indiqué qu'elles avaient eu au moins deux partenaires sexuels au cours des 12 derniers mois, 6 % ont indiqué qu'elles avaient eu au moins un tatouage et 1 % ont indiqué qu'elles avaient utilisé des drogues injectables. Des personnes ayant des partenaires sexuels multiples 84 % n'utilisaient pas des condoms régulièrement.

*Conclusions :* Selon l'analyse sérologique du groupe touché (et des contacts), le taux de séroprévalence estimé de l'HBsAg chez le groupe d'âge étudié se situe entre 0,24 % et 0,47 %. Bien que l'analyse sérologique n'ait pas révélé d'autres cas HBsAg positifs, il y a de fortes possibilités de transmission hétérosexuelle.

# A Population-based Hepatitis B Seroprevalence and Risk Factor Study in a Northern Ontario Town

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In the spring of 1993, a female teenager in a small, northern Ontario town ("Community X") was found to have serologically confirmed acute hepatitis B. Contact tracing revealed five other individuals who had asymptomatic hepatitis B surface antigen (HBsAg) positivity.

As a result of this recently identified hepatitis B cluster, anxiety ran high in Community X, since a local teenager had died from acute fulminant hepatitis B several years earlier. To respond to community concerns and to elucidate the extent and nature of the hepatitis B problem, a population-based vaccination campaign was coupled with a seroprevalence and behavioural risk factor study.

In North America, most cases of hepatitis B infection occur via blood or sexual contact, with infection occurring most commonly in young adulthood. The epidemiology of hepatitis B is changing: the proportion of new cases due to heterosexual exposure and intravenous drug use is

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increasing, while the proportion associated with homosexual transmission is decreasing.<sup>1</sup>

In Canada, 2,762 new cases of hepatitis B were reported in 1993.<sup>2</sup> However, the seroprevalence of hepatitis B in the general population remains unknown, since most serosurveys have been conducted on particular population subgroups or on high-risk populations. For example, of a mixed sex population presenting to a sexually transmitted disease clinic in Barrie, Ontario, 2.7% (5/185) were found to be anti-HBs positive, and no one with hepatitis B infectivity (i.e., HBsAg positivity) was detected.3 By contrast, a 1988/89 serosurvey of 22,911 Ontario prenatal blood specimens found an HbsAg positivity rate of 0.31% (72/22,911) (personal communication; Dr. Margaret Fearon, Virology Section, Laboratory Services Branch, Central Public Health Laboratory, Ontario Ministry of Health; 1993). Nevertheless, these serosurveys do not provide population-based seroprevalence estimates, nor do blood donor, military recruit, institutional, or emergency room serosurvey data.

The present study is different. It represents a true population-based study of both sexes and attempts to define the overall hepatitis B seroprevalence and risk factor rates, within a specified age range, in a community with an index cluster of hepatitis B cases. Linked with the serosurvey was the provision of free vaccine, which served both as a disease prevention measure and as a means to increase sample size.

Community X is a northern Ontario town which lends itself to epidemiological investigation since it is a relatively closed, geographically isolated community. In 1991, the population was less than 4,000;<sup>4</sup> 41% of the population was of British

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descent, 33% French, 5% Portuguese, 4% German, and the remainder "other".5

### **METHODS**

The study was initiated in May 1993. Persons aged 14 to 30 years were targeted for serology determination, risk-factor questionnaire completion, and vaccination.

Following an extensive hepatitis B awareness campaign, as well as liaison with school and community leaders, vaccination clinics were held over the course of three days. In attendance were nursing and clerical staff from the health unit (who provided vaccination, phlebotomy, and data entry services), a physician from the Ministry of Health (who provided public relations and individual counselling services), laboratory staff from the local hospital (who also assisted with phlebotomy services), and community volunteers (who assisted with French translation, crowd management, and age ascertainment). Study participants completed an anonymous questionnaire, and then had blood drawn for hepatitis B serology prior to vaccination. All participants were asked about previous hepatitis B vaccination before receiving the vaccine. Persons with contraindications to the vaccine were encouraged to complete questionnaires and donate blood in order to increase the sample size of the study. Blood samples could not be obtained from two cooperative individuals, who consequently received vaccine in exchange for questionnaire completion only.

# Questionnaire

The 15-item anonymous questionnaire was modelled after a questionnaire used in Nova Scotia to investigate an outbreak of hepatitis B.6 The questionnaire asked for information on gender, age, hepatitis symptoms, and the behavioural risk factors of sexual activity, injection drug use, and tattooing. Responses were later entered on to Epi Info software (version 5; USD Inc., Stone Mountain, Ga.) for analysis purposes. Each questionnaire was linked to a blood sample by a unique four digit code, which was randomly assigned to each study participant.

# Vaccination

Vaccination clinics were scheduled for time zero (mid-May), one month (mid-

TABLE I       Age Breakdown of Serosurvey Participants (n=661) and Age-specific       Serosurvey Participation Rates							
Age* (years)	Number of Serosurvey Participants (A)	Estimated Population† (B)	Estimated Participation Rate (A/B)				
13	9	65	NAS				
14	73	80	91%				
15	68	75	91%				
16	58	60	97%				
17	49	60	82%				
18	56	85	66%				
19	44	80	55%				
20	26	60	43%				
21-25‡	131	315	42%				
26-30‡	131	435	30%				
31-45	9	420	NA§				
Unspecified	7	NA§	NAŠ				

Target ages 14-30

1991 Cersus data projected 2 years forward, assuming stable population cohort Five-year groupings used because of small numbers in specific age cohorts

NA = not applicable

TABLE II Hepatitis B Vaccination Uptake Data for Community X High School	Students
No. of students (Grades 9-13)	321
No. of students aged 14 to 30 inclusive	315
No. of age eligible students vaccinated	277
Proportion of age eligible students not vaccinated	38
Proportion of age eligible students vaccinated as part of seroprevalence study (277/315)	88%
Reasons for age eligible students not being vaccinated through seroprevalence study:	14
no show/no reason	5
travel/school trip	1
yeast allergy	2
illness	5
pregnancy	5
previous vaccination through co-op program	2
sexual contact of index case being followed by family doctor (HBsAg negative)	1
sexual contact of index case (HBsAg positive)	1
familial contact of index case (HBsAg positive)	1
familial contact of index case (anti-HBs positive)	1
familial contact of deceased hepatitis B case (previous immunization)	1
<b>TOTAL</b>	3 <b>8</b>

June), and six months (mid-November) in order to correspond to the school schedule. Contingency plans were made for the provision of vaccine to those persons unable to attend the June or November clinics.

Engerix-B recombinant (yeast-derived) hepatitis B vaccine (SmithKline Beecham Pharma Inc.) was used (1.0 mL, or 20 ug, I.M. in the deltoid). Pregnant women and persons with severe febrile illnesses or allergies to yeast or thimerosal (preservative) were excluded from receiving vaccine.

# Serology

All serum samples were tested for HBsAg (Abbott Auszyme) and all but one for anti-HBs (Abbott Ausab-EIA). Anti-HBs positivity was confirmed by radioimmunoassay (Abbott Ausab), and confirmed positive specimens were subsequently tested for anti-HBc (Abbott Corzyme) to distinguish naturally acquired immunity from that due to prior vaccination. Anti-HBc positive specimens were then tested for IgM anti-HBc in order to determine infection onset. The choice and chronology of serologic testing reflected the regional laboratory's testing capabilities, and they were based on the most cost-effective and efficient method of specimen handling between the regional and central public health laboratories.

By means of a unique four digit code, a study participant could obtain his/her results at the second vaccination clinic. HBsAg positive persons were advised to seek follow-up with the health unit. Anti-HBs positive persons were informed that they did not require additional vaccinations since they had demonstrated evidence of immunity to hepatitis B.

TABLE III Characteristics of Serosurvey Cases Anti-HBs Positive (n=659)*								
Case Number	Age	Sex	No. of Sexual Partners in Past Year	Condom Use	History of STD	Anti-HBc Status (total)	Anti-HBc Status (IgM)	
1† 2 3 4	15 14 27 24	F F M M	1 2-5 1 1	Always Never Sometimes Sometimes	No No Yes	Negative Positive Positive Positive	Negative Positive Negative Negative	

\* No history of previous hepatitis B vaccination.

Given the young age of this individual and assuming no recent HBIG administration, it is possible that this serologic profile represents a false positive anti-HBs due to a low titre, IgM heterotypic antibody. While individuals exposed to HBV can be positive for anti-HBs alone, such a serologic profile more typically exists in persons who have had chronic hepatitis B for many years and in whom the anti-HBc titre has fallen to undetectable levels.

Se	rosurvey		TABLE IV nts Reporting History of Sexual Intercourse, by Selected Ages*							
Age		Aale		emale		h Sexes				
14	%	(sample size)	%	(sample size)	%	(sample size)				
14	6	(n = 30)	12	(n = 43)	10	(n = 73)				
15	19	(n = 36)	50	(n = 32)	34	(n = 68)				
16	50	(n = 28)	52	(n = 30)	52	(n = 58)				
17	71	(n = 21)	75	(n = 28)	74	(n = 49)				
18	76	(n = 29)	65	(n = 26)	71	(n = 55)				
19	74	(n = 23)	91	(n = 21)	82	(n = 44)				
20	94	(n = 17)	78	(n = 9)	89	(n = 26)				
* Note: Nor sexual inte		ne 13-year-olds wl	ho provi	ded blood specime	ens repo	orted ever having had	d			

#### Case definition

Evidence of hepatitis B infection was defined as serological positivity for (1) HBsAg, (2) anti-HBs *and* anti-HBc, or (3) anti-HBs in the absence of prior vaccination or HBIG administration.

# RESULTS

Six hundred and seventy-three persons completed risk factor questionnaires, and of these, 661 persons (331 males, 330 females) submitted blood samples for hepatitis B serology. Six hundred and sixty persons were vaccinated. Although the target group for vaccination and serosurvey purposes was persons aged 14 to 30, questionnaire age responses revealed that 18 persons outside this age range were also included in the study. These age ineligible persons and seven others who did not specify their age were excluded from further questionnaire analysis. Table I shows the age breakdown of persons providing serum specimens and the estimated age-specific submission rates. Table II details the vaccination uptake data for high school students.

Of the 661 blood specimens submitted, none was found to be HBsAg positive. Five

persons were found to be anti-HBs positive, but one of these had been vaccinated previously. Table III provides details of the four anti-HBs positive persons who denied previously having received hepatitis B vaccine. These were all heterosexual, and one had IgM antibodies to HBc; none reported having jaundice or dark urine, receiving a tattoo, or using injection drugs within the previous year. No statistically significant differences were found between anti-HBs positive and negative persons in terms of gender, number of sexual partners, condom use, or sexually transmitted disease (STD) history. This was not unexpected, given the small number of serologically positive cases.

Six-hundred and thirty-six persons known to be aged 14 to 30 completed a risk factor questionnaire and submitted a blood sample for hepatitis B serology (317 males, 319 females). This represents an estimated sample size of 51% (636/1240, where 1240 represents the current estimated population of persons aged 14 to 30 in Community X, based on 1991 Census agecohort figures projected two years forward). Forty persons (26 males, 14 females; n = 634) reported having received at least one tattoo within the previous year; 20 received a tattoo in Community X, 2 in the nearest city (Thunder Bay), 17 elsewhere in Ontario, and 2 out-of-province. Six persons (n = 634) acknowledged illicit injection drug use in the previous year, one of whom also shared needles. One male (n = 311) and three females (n = 199) reported a history of homosexual activity. High rates of sexual activity among teenagers (with over 50% of 16-year-olds reporting a history of sexual intercourse) are shown in Table IV.

Nineteen percent (122/635) reported two or more sexual partners in the previous year, and 3% (10/317) of males reported six or more partners (Table V). Of participants with two or more sexual partners in the previous year, only 16% (19/120) reported always using condoms during intercourse, and another 16% (19/120) reported never using condoms. Five percent (12/221) of sexually experienced males and 6% (13/224) of sexually experienced females reported having had a sexually transmitted disease; these figures may be underestimates of the true STD burden of illness, since several respondents wrote on the questionnaire that they did not know what diseases are considered to be sexually transmitted.

# DISCUSSION

Despite community and investigator expectations to the contrary, the serosurvey did not reveal a "hidden reservoir" of hepatitis B infection in Community X (at least not in the population aged 14 to 30 years). No cases of HBsAg positivity were detected beyond those discovered as a result of contact tracing related to the index case. Furthermore, IgM anti-HBc

TABLE V Sexual Activity in Previous Year for Serosurvey Participants Aged 14 to 30*														
Number of Sexual Partners														
Gender	None	(%)	One	(%)	2-5	(%)	6-10	(%)	>10	(%)	Unspecified	(%)	Totals	(%)
Male	92	(29)	138	(44)	67	(21)	5	(2)	5	(2)	10	(3)	317	(100
Female	94	(30)	177	(56)	43	(14)	2	(1)	0	(0)	2	(1)	318	(100
Both sexes	186	(29)	315	(50)	110	(17)	7	(1)	5	(1)	12	(2)	635	(100

testing revealed evidence of only one recent infection (since IgM antibody lasts for 4 to 6 months after infection).<sup>7</sup> These serological results suggest that hepatitis B infection in Community X remained largely confined to the original cluster, in which the predominant risk factor appears to have been familial association.

While the use of mass community vaccination as a hepatitis B control measure may be questioned in light of the serological results, it is likely that such intervention served to limit the spread of hepatitis B infection in Community X. Follow-up of the anti-HBs cases revealed one that was epidemiologically linked by heterosexual activity to the original cluster. In the absence of the rapid vaccination campaign, further serological testing may have disclosed a substantially greater burden of hepatitis B infection given the extent of behavioural risk factors in the community.

The strength of this study is its yielding of a population-based estimate of hepatitis B seroprevalence (for persons aged 14 to 30 years) in an isolated, northern Ontario town. When appropriately aged persons from the initial cluster investigation are considered, an HBsAg seroprevalence rate of between 0.24% (3/1240, where the denominator denotes target population) and 0.47% (3/641, where the denominator denotes study participants plus cluster/contacts) can be estimated for the age cohort. (This estimated seroprevalence rate is consistent with the results of the 1988/89 Ontario prenatal serosurvey.) Similarly, the anti-HBs seroprevalence rate attributable to infection (as opposed to vaccination) is estimated to be between 0.40% (5/1240) and 0.78% (5/641). While the potential biases inherent in client self-selection for serological testing must be acknowledged, the anonymous nature of the serum testing coupled with the highly popular provision of free vaccine resulted in impressive sample sizes (at least

51% of the total eligible population and 88% of the high school population). Since public health officials were familiar with the serologic results of the original cluster and contacts (i.e., those persons presumed to be at highest risk of hepatitis B), it is likely that the seroprevalence estimates arising from the serosurvey result accurately reflect the hepatitis B situation of the overall target population. The high community participation rate attests to the feasibility and usefulness of the three-pronged study approach i.e., serosurvey, questionnaire, and vaccination.

The study provides prevalence information on several behavioural risk factors. Of particular note is the early age of sexual activity in Community X. In the Ontario Health Survey (1990), 38% of all respondents then aged 16 to 24 reported having had sexual intercourse by age 18;<sup>8</sup> the comparable percentage for residents of Thunder Bay District Health Unit territory was 52%.<sup>9</sup> In Community X, 52% (30/58) of 16-year-olds participating in the serosurvey reported having had intercourse. This indicates a need for early sexual education.

Further research is needed to assess the generality of the findings on injection drug use, tattooing, and condom use, because these activities have broad implications for public health programming in health promotion and disease prevention. Conducting a detailed behavioural risk factor study in a town comparable to Community X without an index hepatitis B cluster would serve this purpose.

# ADDENDUM

Population compliance was monitored regarding receipt of the second and third doses of hepatitis B vaccine. Of the persons vaccinated during the clinics held in May 1993, 93% (611/660) received a second dose of vaccine in June (573 from health unit sponsored clinics and 38 from family

physicians) and 76% (505/660) received a third dose of vaccine (429 from clinics and 76 from physicians). Given the intensity of local advertising efforts and the high level of community awareness, this compliance monitoring may provide useful information for jurisdictions considering universal hepatitis B vaccination programs.

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