Cost without benefit? The introduction of hepatitis B vaccine in Canada

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The development of hepatitis B vaccine is an important landmark in preventive medicine. With this safe and highly efficacious immunizing agent we may now be able to protect susceptible individuals from infection.[1,2] The vaccine will prevent more than acute disability, however. It will help to reduce the development of chronic hepatitis, cirrhosis and primary hepatocellular carcinoma — conditions that account for most of the morbidity and mortality associated with hepatitis B. Thus, this vaccine should rightly be heralded with enthusiasm. But our expectations must be tempered by the knowledge that the vaccine's high cost and limited supply might curtail the scope of its benefits.

Hepatitis B vaccine (Heptavax-B, Merck, Sharp & Dohme) is unique in several respects. Unlike other antiviral vaccines, which are prepared through laboratory cultivation of the specific viruses, this vaccine is derived from hepatitis B surface antigen (HBsAg) particles that are obtained from the plasma of healthy human carriers.[3] The raw HBsAg material is subjected to three separate purification processes, any one of which will inactivate the hepatitis B virus, as well as representatives of all known virus groups.[3]

Recently, however, concern has arisen over the long-term safety of this vaccine with respect to a newly recognized disorder, acquired immunodeficiency syndrome (AIDS).[4-6] The epidemiologic features of AIDS support the hypothesis that an unidentified and uncharacterized blood-borne infectious agent may be an etiologic factor in the underlying immunologic defect.[4,5] It would be virtually impossible though, for the purported agent to survive the extensive and elaborate purification procedures employed in the production of hepatitis B vaccine. Furthermore, in response to speculation about the possible transmission of AIDS, a recently convened committee of experts re-evaluated the safety of the vaccine. They reviewed three vaccine–placebo trials that showed no cases of AIDS among 1927 vaccinees; as yet, no adverse long-term reactions have been reported.[7] Finally, clinical trials of the vaccine's efficacy have demonstrated conclusively that development of the antibody to HBsAg (anti-HBs) following vaccination is synonymous with protection against the virus and its consequences.[1,2]

Initially, only individual recipients of the vaccine will be protected from infection, but in the long run the community should benefit from a reduction in the total burden of chronic disease related to hepatitis B virus infections. These long-range benefits will be expressed in terms of savings in human and financial costs.

In contrast to the situation in developing countries, where socioeconomic standards create an environment that favours transmission of the virus and predisposes the majority of the population to a significant risk of infection,[8] the average Canadian citizen is not at risk. Therefore, we do not require a universal vaccination program in Canada. Recently, however, steadily increasing rates of hepatitis B have been reported in this country, indicating that the disease is a growing problem in our population.[9] The persistence of the disease and the growth in the number of infections in industrialized nations such as Canada are related to the subtle ways the virus can spread and to the existence of the chronic, asymptomatic carrier state. Chronically infected people are frequently unaware of their condition and, consequently, those who are exposed to the blood, semen and saliva of these carriers do not know that they risk being infected. It is the people who are exposed, however, who would benefit most from immunization with the new vaccine.

We estimate that there are now 1.3 million people, or at least 5% of Canada's population, at risk of hepatitis B (Table I). The diversity of this group is reflected by variations in the risk of infection in the different subgroups. Obviously, then, the potential for transmitting infection is also subject to wide variation. With regard to vaccination, individuals in the subgroups are not equally identifiable or accessible.

Our society is already incurring significant costs as a result of the presence of hepatitis B in our population. In 1977 an estimate of the annual cost of hepatitis B infections in Canada, based on the related premature deaths, hospitalizations and lost productivity, was $31.7 million.[9] This figure can be expected to escalate as the chronic sequelae of an increasing number of infections become clinically evident. The pool of chronic carriers will continue to grow — if the transmission of hepatitis B virus continues unchecked.

Considering the diverse nature of our at-risk population, this forecast presents a major challenge for those who consider it their responsibility to protect individuals and the whole community when effective means are available. In mounting such an effort, there must be a clear commitment to work toward the goal of a substantial reduction in the morbidity and mortality associated with hepatitis B in our country. The new vaccine provides a valuable tool that, when coupled with cur-

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rently practised measures of environmental control, could contribute greatly. This goal can be reached more readily with a comprehensive vaccination program that attempts to identify and immunize all susceptible at-risk individuals. This would require collaboration and co-operation among the organizations and networks that represent or foster the health of our population. Unfortunately, some of the at-risk groups are not represented by any structure or organization, and we would have to ensure that these groups are not neglected in the planning and implementation of an immunization campaign.

Initially, certain practical factors would limit the scope and direction of a comprehensive campaign. The supply of vaccine to Canada will be limited for several years, and it would probably be allocated according to priorities based not solely on estimates of risk but also on the ease of identification and the accessibility of potential recipients (health care workers in frequent contact with blood, for example, as opposed to infants of carrier women). Recently the Advisory Committee on Epidemiology[46] published guidelines on the priorities, allocation and control of the vaccine supply in Canada.

Table I—Groups at risk of exposure to hepatitis B in Canada

Groups at risk	Estimated population (thousands)	Prevalence of hepatitis B markers (%)
Patients		
With hemophilia and related disorders[10-12]	2.0	76–96
With thalassemia[13]	0.6	25–90
Undergoing dialysis[14,15]	5.5	42–59
Infants of women with hepatitis B surface antigen[16,17]	?	47–91
Intravenous drug users[18-20]	60.0	50–71
Pediatric cancer patients[21]	?	18
Adult cancer patients[22]	?	21–32
Alcohol-dependent patients[23,24]	?	18–32
Residents of institutions		
Mentally retarded[25]	22.0	50–80
Prisoners[26]	19.8	42
Occupational		
Health care: medical, paramedical, dental, paradental, laboratory, all students[27-34]	310.0	7–58*
Staff in institutions for the mentally retarded[25]	25.0	8–12
Morticians and embalmers	2.5	?
Ethnic groups		
Native Indians[35]	300.0	8–61†
IndoChinese[36,37]	?	51–59
Black Africans[37,38]	?	44–75
Pacific Islanders[39]	?	30–88
Other		
Male homosexuals[40,41]	400.0	60–68
Promiscuous heterosexuals[41,42]	?	15–31
Household contacts of carriers or patients[43,44]	141.0	26–61
Total	1288.4	

*The category at highest risk appears to be staff attending hemodialysis patients.[28] The risk is directly associated with the frequency of contact with blood or blood-related equipment, and this, for the most part, accounts for the wide variation.[29-31] The average prevalence across all health care groups is 12% to 26%.[45]
†This wide range appears to be related to the variation in the basic level of hygiene in individual communities.[35]

Primarily the committee addressed the immediate use of this vaccine and suggested no guidelines for its long-term use. Since the committee did not discuss the issues of investigating the possible vaccine requirements of as yet unexamined groups, there must be a concurrent effort to determine these needs and develop vaccination programs for groups whose members are not identified easily and where valid data are lacking or incomplete. It may be necessary to promote and fund epidemiologic studies. The most effective strategies may not be developed, however, unless pilot projects first demonstrate the feasibility and success of various approaches to these less accessible groups.

The fundamental issue of payment for the vaccine, which will cost about $125 for each individual, could severely restrict the implementation of a comprehensive program if the recipient were required to pay. To avoid administering this costly vaccine to large numbers of previously infected individuals, for whom there are no benefits, screening has been recommended in a number of the groups in which exposure and infection rates are high.[3,27] It would appear to be unreasonable to encourage at-risk individuals to submit to screening and then to demand that they pay for the vaccine. Such a policy would discourage compliance in those who should be vaccinated.

One alternative to a rationally planned vaccination program, with its necessary control of vaccine distribution, is an open marketplace situation, where informed individuals or their representatives, interested organizations and institutions may compete for portions of the available supply if they consider that the expenditure is warranted. Quite clearly this would lead to an inequitable distribution of the vaccine. The more organized and institutionalized sectors of the at-risk population could well monopolize the supply of vaccine. Not only would this be socially irresponsible, but also it would impede any future initiatives and might produce minimal overall benefits while adding considerable cost.

In summary, it appears that the introduction of hepatitis B vaccine could substantially reduce the burden of disease related to the hepatitis B virus. Recent cost-effectiveness studies have demonstrated that rational use of this new vaccine can result in substantial savings in health care costs alone.[45,47] These analyses assume that sizeable portions of the various high-risk groups will be protected by vaccination. Should certain groups be neglected, continuing costs will be incurred as new infections arise in these groups.

To realize the long-range benefits possible with this vaccine, it will be necessary to resolve a number of problems and issues. This will be done best through the planning of a collaborative and comprehensive hepatitis B vaccination program that includes a commitment of resources, both financial and human.[9] Without this commitment it is very possible that the use of this vaccine in Canada will result in additional costs, yet no long-range benefits.

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