Role of screening in prevention and treatment

M Kane, M Alter, R Esteban, M Rizzetto

Abstract

Since viral hepatitis may be the most common form of chronic viral disease in the world, strenuous attempts are being made to reduce the incidence. To achieve this, strategies are being developed by various national and international bodies involving both the immunisation and screening of certain groups of the population. These strategies are by no means universal, and the value of screening specific groups is the subject of much debate. This paper will address a number of the issues related specifically to the question of screening for hepatitis B virus and hepatitis C virus (HBV and HCV, respectively) namely (a) what is screening?; (b) why should we consider screening?; (c) who should we consider screening?; (d) what are the benefits and liabilities of screening?; (e) what constitutes an acceptable screening test?; (f) should we be screening for HBV or HCV?

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What is screening?

'Screening' may be defined as the routine investigation of an apparently healthy population to detect an unsuspected condition for which treatment would be beneficial. The two crucial issues are whether our tools for 'detection' are good enough, and whether our 'treatment' is sufficient to justify consideration of screening.

Why should we consider screening?

Screening has three main benefits: firstly, the ability to identify people with a medical condition that can then be treated; secondly, to prevent further infection or transmission; and thirdly, as a prevaccination measure.

Who should we consider screening?

The universal screening of groups such as pregnant women in developed countries plays a significant role in the strategy to control hepatitis B virus (HBV) infection. Screening is justified because 'treatment' of infants of carrier mothers is highly effective in preventing the infants from becoming HBV carriers. Some programmes screen immigrants and refugees from areas of high endemicity so that susceptible family contacts may be vaccinated.

While the screening of blood and blood products is now an accepted and important component in any national programme for the control of HBV and hepatitis C virus (HCV), the question of screening individuals in so called high risk groups, among health care workers, and even the general population is less straightforward. Legal, ethical, and economic considerations impact on the principle of any broadly based screening programme.

What are the benefits and liabilities of screening?

Early detection would allow possible treatment of the condition at an early stage, reduce the likelihood of transmission to others, and also assist in the identification of infected individuals in the family.

The liabilities associated with screening include the legal, ethical, and economic considerations referred to earlier. The dilemma presented by a false-positive or false-negative result can lead to unnecessary medical investigations, incorrect counselling advice, and possible psychological damage. A positive test can lead to job loss and compromise of the individual's insurability. The whole issue also needs careful management in terms of medicolegal liability. Even properly diagnosed patients may undergo expensive, unpleasant treatment without medical benefit.

What constitutes an acceptable screening test?

The sensitivity, specificity, and predictive value of the tests available are crucial when trying to assess candidate screening tests. Unfortunately, the characteristics of the tests available mean that false-positives and false-negatives are currently inevitable (Fig 1). The challenge is therefore to minimise the false-positives and false-negatives by designing tests that clearly separate infected and uninfected populations (Fig 2).

Should we screen the general population for HCV?

There are several issues that need to be taken into consideration when a new screening test is introduced, particularly into the general population, namely:

(a) Are we screening for an important public health problem? In the USA, HCV is an important problem. Approximately 150 000 acute infections occur annually, and over 60% of these individuals develop chronic liver disease. It is estimated that 8–10 000 deaths occur each year as a result of hepatitis C;

(b) Is there an accepted treatment or an intervention that can prevent transmission if we do identify individuals who are infected? Interferon alfa is licensed for the treatment of

Division of Communicable Diseases, World Health Organization, Geneva, Switzerland
M Kane

Centers for Disease Control, Atlanta, Georgia, USA
M Alter

Liver Unit, Hospital Universitario Vall d'Hebrón, Barcelona, Spain
R Esteban

University of Turin, Turin, Italy
M Rizzetto

Correspondence to:
Dr M Kane, Department of Communicable Diseases, World Health Organization, Geneva, Switzerland.

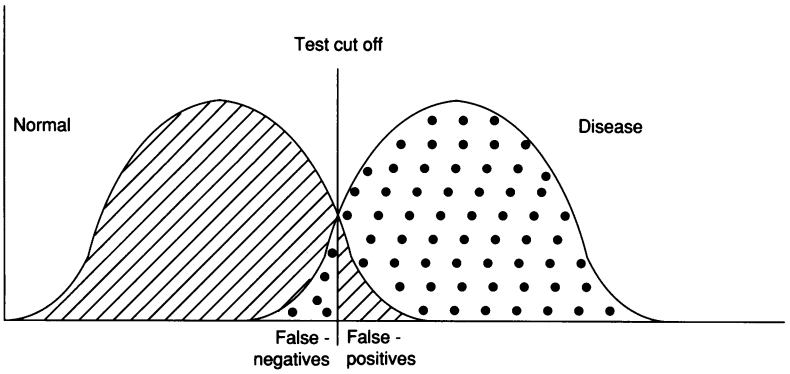

Figure 1 Characteristics of the screening tests available mean that false-positives and false-negatives are currently inevitable.

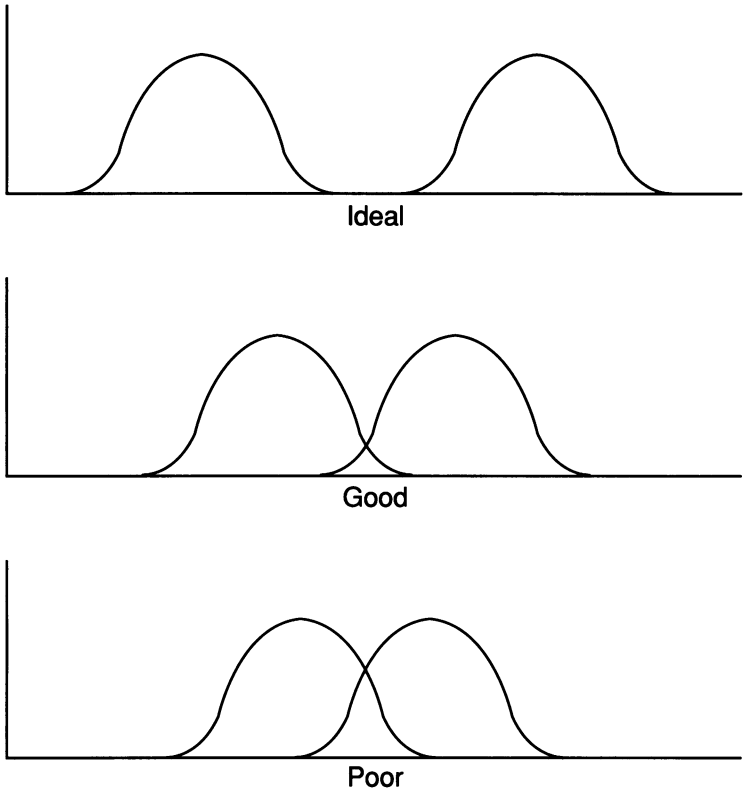

Figure 2 The challenge to minimise false-positive and false-negative results.

chronic hepatitis C, but a good response to treatment occurs only in about 50% of patients. Relapse after stopping treatment is high, and there are no defined markers for resolution of disease or infection;

(c) Are facilities available for diagnosis and treatment for individuals identified as infected? There are facilities for the diagnosis and treatment of anti-HCV patients in many countries, although the cost of these procedures may be prohibitive;

(d) If we screen will we diagnose the disease earlier and will earlier treatment result in a better outcome? The natural history of hepatitis C has not been adequately defined, so it is difficult to identify a point in the history of the disease where treatment or intervention will be more effective;

(e) Is there a suitable test and is the test acceptable to the population being screened? There is no true confirmatory test for the presence of HCV. The positive predictive value of commercially available tests for anti-HCV when used to screen low risk populations is less than 50%;

(f) Have we agreed upon a policy of who to treat or is there a consensus on what recommendations we should make for preventing transmission between infected individuals? In general, treatment for chronic hepatitis C is being offered to patients with biopsy proved chronic active hepatitis or cirrhosis without decompensated liver disease, or to those with persistent hepatitis who are symptomatic. Except for the donor setting, there are insufficient data and little agreement on recommendations for the prevention of person to person transmission of HCV, particularly with respect to sexual activity;

(g) Have we established the costs and benefits of screening and subsequent treatment or intervention? Are early diagnosis and treatment balanced economically against the cost of medical care for the disease if we were not to screen or treat? Studies have yet to establish the costs and benefits of screening and treatment.

Screening of blood donations for anti-HCV

The screening of blood donations for anti-HCV has had a direct impact on the decrease of blood transfusion associated hepatitis. It has also had an indirect effect in providing important information regarding the epidemiology and knowledge of the disease.

From July 1989 to April 1990 more than 30 000 consecutive blood donors were tested in the Hospital Universitario Vall d'Hebrón, Barcelona, Spain; 368 of them were found to be anti-HCV positive, that is an incidence of 1·2%. The incidence of transfusion associated hepatitis seen in Barcelona before anti-HCV screening was 9·6%. With retrospective anti-HCV testing we predicted that the risk of acquiring transfusion associated hepatitis in a recipient of an anti-HCV positive unit was 137 times higher than the risk of a recipient of an anti-HCV negative unit. When anti-HCV screening was implemented we could also prospectively assess an 80% reduction in transfusion associated hepatitis cases with a donor loss of 1·1%.

Anti-HCV screening has allowed the identification of anti-HCV positive donors whose liver biopsy specimens have given useful information regarding the liver lesions of asymptomatic HCV infection. For example, 59% of 100 RIBA-2 positive donors had chronic active hepatitis, 15% hepatic cirrhosis, and 20% chronic persistent hepatitis. These data have provided a better understanding of HCV infection and have highlighted a high number of possible candidates for antiviral treatment.

Screening for anti-HCV within the family

Virtually every day practising physicians are faced with an anti-HCV positive patient with some form of liver disease. It is relatively

easy to recommend a liver biopsy and then treatment if he or she has some form of liver pathology. It is much more difficult to offer advice, however, about testing for anti-HCV within the family.

By making recommendations about testing for anti-HCV, the physician takes a degree of personal responsibility for the patient, not only in terms of cost but, in the event of an incorrect diagnosis, psychological damage to the patient and family. Furthermore, since viraemia does not necessarily imply liver disease, it is difficult to explain the pathobiological importance and implications of a positive test.