A WWW-accessible knowledge base for the interpretation of hepatitis serologic tests

C. Chizzali-Bonfadin *, K.-P. Adlassnig, M. Kreihsl, A. Hatvan, W. Horak

Department of Medical Computer Sciences, University of Vienna, Spitalgasse 23, A-1090 Vienna, Austria

Abstract

HEPAXPERT is a knowledge-based system that interprets the results of routine serologic tests for infection with hepatitis A and B viruses. The following tests are included: hepatitis A virus anti-bodies (anti-HAV), IgM antibodies to the hepatitis A virus (IgM anti-HAV), hepatitis A virus (HAV in stool, hepatitis B surface antigen (HBsAg) and antibodies (qualitative anti-HBs, quantitative anti-HBs titre), antibodies to hepatitis B core antigen (anti-HBc and IgM anti-HBc), and hepatitis B envelope antigen (HBeAg) and antibodies (anti-HBe). HEPAXPERT/WWW – an implementation of HEPAXPERT-III for WWW- can be reached by URL http://www.swun.com/hepax of the World Wide Web. After selecting HEPAXPERT/WWW, serologic test results can be entered and will be transferred as an e-mail message for subsequent interpretation which is done off-line with HEPAXPERT-III. The textual interpretation is sent back via e-mail. Each qualitative test for hepatitis A and B antibodies and antigens may produce one of four possible results: positive, negative, borderline, and not tested. To cover the resulting 64 (A) and 57 344 (B) combinations of findings, the knowledge base of HEPAXPERT/WWW contains 16 rules for hepatitis A and 131 rules for hepatitis B serology interpretation. This basic knowledge is structured such that all possible combinations of findings can be interpreted and there is no overlap in the premises underlying the rules. The reports that the system automatically generates include: (a) the transferred results of the tests; (b) a detailed analysis of the results, including virus exposure, immunity, stage of illness, prognosis, infectiousness, and vaccination recommendation; and (c) optional: an ID to distinguish the origin of the interpretation requests. © 1997 Elsevier Science B.V.

Keywords: Expert system; World Wide Web; Hepatitis serology; HEPAXPERT-III

1. Introduction

HEPAXPERT/WWW is an implementation of HEPAXPERT-III [1] for WWW.

HEPAXPERT-III—the successor of HEPAXPERT-I [2,3] and HEPAXPERT-II [4,5]—is an expert system that interprets the results of qualitative and quantitative routine serologic tests for infection with hepatitis A and B. The tests measure antibody to the

* Corresponding author. Tel.: + 43 1 404006666, fax: + 43 1 404006667; e-mail: ccb@akh-wien.ac.at

hepatitis A virus (anti-HAV), IgM antibody to hepatitis A virus (IgM anti-HAV), hepatitis A virus (HAV) in the stool, hepatitis B surface antigen (HBsAg) and antibody (both qualitative anti-HBs and quantitative anti-HBs litre), antibodies to hepatitis B core antigen (anti-HBc and IgM anti-HBc), and hepatitis B envelope antigen (HBeAg) and antibody (anti-HBe). The HEPAXPERT-III system automatically provides and interprets the result of these tests, without the use of additional biochemical or clinical data, and thus helps physicians to understand complex serologic findings.

2. Methods

Each qualitative test for hepatitis A and B antibodies and antigens may produce one of four possible results: 'positive', 'negative', 'borderline', or 'not tested'. The quantitative anti-HBs titre test can either have the result 'not tested' or may fall into one of the following 14 titre-ranges: [0], [1, 10], [11, 34], [35, 79], [80, 249], [250, 499], [500, 999], [1000, 1999], [2000, 3999], [4000, 6999], [7000, 11 999], [12 000, 24 999], [25 000, 49 999], and [50 000, 99 999]. Because there are three qualitative tests for hepatitis A (anti-HAV, IgM anti-HAV, and HAV in the stool) and six qualitative tests plus one quantitative test for hepatitis B (HBsAg, anti-HBs, anti-HBc, IgM anti-HBc, HBeAg, anti-HBe, and anti-HBs titre), there are 64 (4^3) possible combinations of findings for hepatitis A, and 57 344 ((4^6) × 14) possible combinations for hepatitis B serology test results. With HEPAXPERT-III, each combination is associated with one specific textual interpretation.

To deal with the 64 and 57 344 possible combinations of findings, the knowledge base of HEPAXPERT-III contains 16 rules for hepatitis A and 131 rules for hepatitis B

interpretation. These rules were defined for various purposes. For hepatitis A, we developed 13 rules to interpret the given combination of test results (interpretation step) and three rules to add specific advice, if necessary (completion step). In the more complex situation of hepatitis B, 11 rules combine the qualitative anti-HBs and the quantitative anti-HBs titre test results (preprocessing step), 115 rules establish an interpretation of the then given combination of findings (interpretation step), and five rules are applied to insert selected data items and add specific advice (completion step). The interpretation rules for hepatitis A and B serology are structured such that all possible combinations of findings can be interpreted and there is no overlap in the premises underlying these rules. Thus, the rules occasionally group a very high number of combinations of findings into one category of interpretation. An example of an interpretation rule for hepatitis B serology is given in Fig. 1.

A fictitious test, called anti-HBs-SUM, — to be used in the conclusions of the rules combining the qualitative anti-HBs and the quantitative anti-HBs titre test results—is introduced. This test can not only assume +, −, ±, and * but also the values I_1 = 'in interval [1, 10]', I_2 = 'in interval [11, 34]', I_3 = 'in interval [35, 79]', and I_4 = 'in interval [80, …]'.

In analyzing serologic test results, the HEPAXPERT-III program compares the constellation of serologic findings with constellations that may occur in the course of hepatitis A or B infection. Possible active or passive immunization is taken into account as well. However, there are several possible sources of misinterpretation, such as deviations in the course of the disease from the assumed courses, as well as falsely positive and falsely negative findings. Therefore, in

IF

HBsAg	anti-HBs-SUM	anti-HBc	IgM anti-HBc	HBeAg	anti-HBe
- ± *	+ I_1 I_2	± *	-	- ± *	- ± *

THEN

This constellation of findings (positive anti-HBs antibodies, with negative IgM anti-HBc antibodies) indicates the presence of immunity to the hepatitis virus B. This immunity may either have been acquired naturally upon restitution following a hepatitis B virus infection or may have been induced by active or passive immunization.

<u>Vaccination recommendation</u>: If an indication for a hepatitis B vaccination exists, the primary course of immunization has been completed, and the last partial vaccination was given at least 1 month previously, an immediate hepatitis B booster shot is recommended to maintain the immunity. If the person is suspected of being a 'low responder' a titre check 2 months after the booster is advisable.

Fig. 1. An example of a rule for hepatitis B serology interpretation. The premise of the rule should be read as follows: +, 'positive'; −, 'negative'; ±, 'borderline'; and *, 'not tested'. Several entries in one table element are connected by an 'or', several table elements in one row are connected by an 'and'.

each case the program's conclusions have to be correlated with the patient's overall clinical picture.

HEPAXPERT/WWW can be reached by URL http://www.swun.com/hepax of the World Wide Web. After selecting HEPAXPERT/WWW, serologic test results can be entered and will be transferred as an e-mail message for subsequent interpretation which is done off-line with HEPAXPERT-III. The textual interpretation is sent back via e-mail.

3. Results

The reports that the system automatically generates include (a) the transferred results of the tests, (b) a detailed analysis of the results, including virus exposure, immunity, stage of illness, prognosis, infectiousness, and vaccination recommendation, and (c) optional: an ID to distinguish the origin of the interpretation requests. In clinical use the physician providing the specimen for testing is free to request individual findings; in addition, the laboratory is permitted to issue findings that are not unambiguously positive or negative, so that it will be possible to interpret incomplete and uncertain results as well as prototypical results. Furthermore, as a check on the laboratory results, any inconsistent combinations of findings are identified. It is thus possible to review the findings before they are transmitted to the ward.

The HEPAXPERT-I and -II programs has been in routine use at the hepatitis laboratory of the University of Vienna Medical School since September 1989. The structure of the knowledge base has resulted in an exceptionally practice-oriented and efficient interpretation program, among whose merits are convenient data input and interpretation of findings in a matter of seconds. Its acceptance among physicians is high.

HEPAXPERT/WWW is available since August 1995 and there are up to ten requests per week. In August 1996 the interpretation process of HEPAXPERT/WWW was changed from HEPAXPERT-I to HEPAXPERT-III to enhance the system with the quantitative anti-HBs titre test result which is then used to make vaccination recommendations.

4. Requirements

HEPAXPERT/WWW can be accessed from (presumable) any WWW-browser and through (presumable) any e-mail-system.

References

[1] K.-P. Adlassnig, C. Chizzali-Bonfadin, M. Kreihsl, W. Horak, A Computerized System for the Interpretation of Serologic Tests for Hepatitis A and B. LabMedica Int. 1–2 (1995) 18–19.

[2] K.P. Adlassnig, W. Horak, HEPAXPERT-I: automatic interpretation of tests for hepatitis A and B, MD Comput. 8 (1991) 118–119.

[3] K.-P. Adlassnig, W. Horak, Development and retrospective evaluation of HEPAXPERT-I: a routinely-used expert system for interpretive analysis of hepatitis A and B serologic findings, Artif. Intell. Med. 7 (1995) 1–24.

[4] K.-P. Adlassnig, W. Horak, C. Chizzali-Bonfadin, Integrated medical database and expert system HEPAXPERT-II: automatic interpretation of tests for hepatitis A and B, in: Proc. Medical Informatics Europe 1991 (MIE'91), Springer-Verlag, Berlin, 1991, p. 1041.

[5] K.-P. Adlassnig, W. Horak, C. Chizzali-Bonfadin, Automatic interpretation of tests for hepatitis A and B: the integrated medical database and expert system HEPAXPERT-II, Med. Focus Int. 3 (1994) 26–29.

.