Viral Hepatitis B and C
The Changing Concept for Thailand

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Topics

- Identification of patients at risk for HBV, HCV
- Evaluation of patients for HBV, HCV
- Selection of drugs
- HBV treatment in special groups
  - Immune tolerance
  - Healthcare workers
  - Pregnancy
- HCV patients who require after SVR follow-up
- Conclusion

The burden of HBV: approximate number of HBV carriers by age

Age (yrs)	Number compared with the actual population			
	Population	% HBV carrier rate		Number of HBV carriers§
<5	3,735,837	0.10		3,875
5–10	4,750,137	0.29		13,889
11–20	8,829,060	0.69		61,313
21–30	9,330,783	2.97	Born before 1992	277,289
31–40	10,346,437	3.77		389,671
41–50	10,465,811	4.66		488,043
51– >60	16,496,285	5.99		988,459
Total	**63,954,350**	**3.48***		**2,222,540**

§ Calculated from % HBV carrier rate in each age group multiplied by the population for each age group.
* Defined as the % HBV carrier rate calculated from the total number of HBV carriers (2 222 540) compared to the total Thai population of 63 954 350.

Posuwan N, Wanlapakorn N, Sa-nguanmoo P, et al. Plos one 2016

HCV infection decreased by half from 715,930 people in 2004 to 356,670 people in 2014

	Year 2004					Year 2014				
Age range	Anti-HCV +ve rate	RNA +ve rate	Thai population	Anti-HCV carrier	HCV carrier	Anti-HCV +ve rate	RNA +ve rate	Thai Population	Anti-HCV carrier	HCV carrier
0–10	1.47	0.41	9,553,008	140429	39,244	0.35	0.05	8,485,974	29701	4,273
11–20	1.42	0.53	9,419,566	133758	50,238	0.59	0.10	8,829,060	52091	8,699
21–30	2.28	1.02	10,570,790	241014	107,318	0.45	0.00	9,330,783	41989	0
31–40	2.56	1.92	10,972,787	280903	210,745	1.04	0.13	10,346,437	107603	13,472
41–50	3.10	1.55	8,859,873	274656	137,540	2.72	1.69	10,465,811	285061	176,466
>50	3.36	1.53	11,173,300	375423	170,846	1.46	0.93	16,496,285	242495	153,760
Total	**2.15**	**1.00**	**60,549,324**	**1,446,183**	**715,930**	**0.94**	**0.39**	**63,954,350**	**758,940**	**356,670**

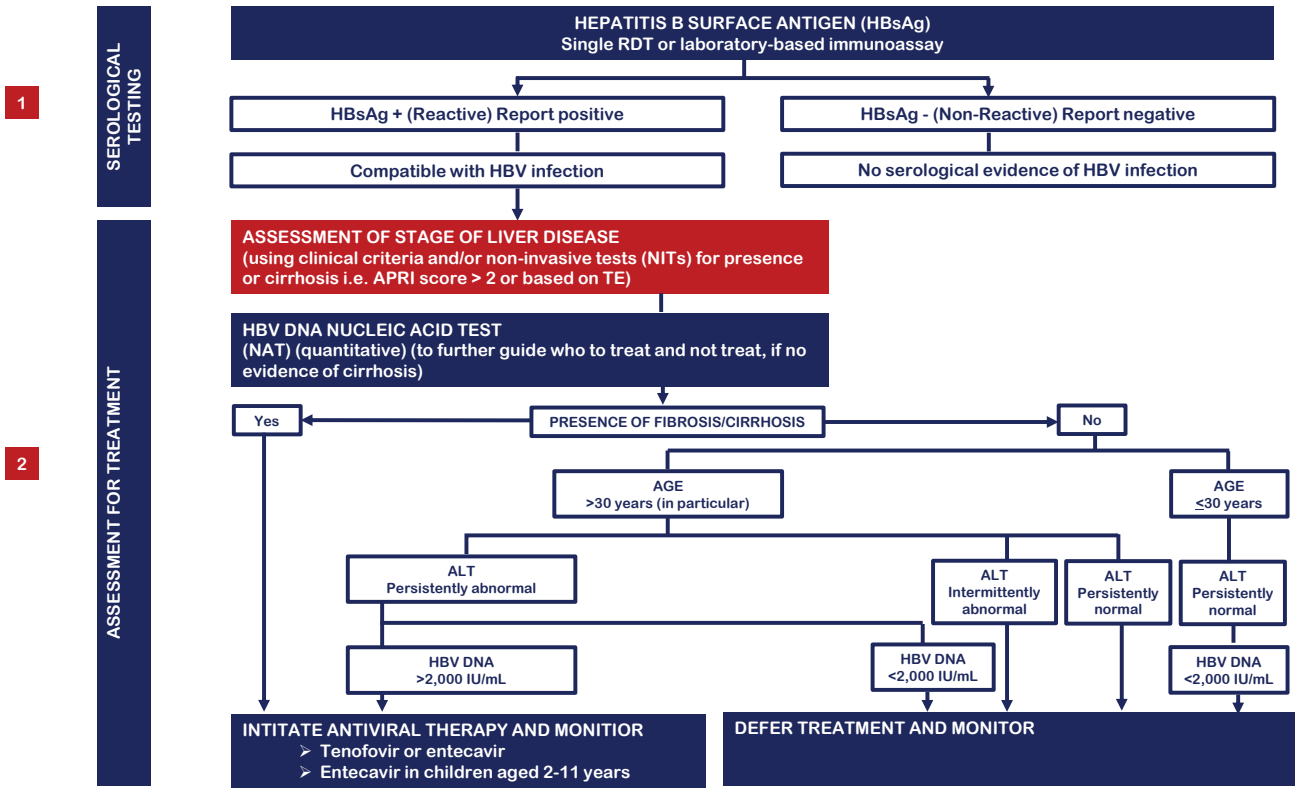
About 260,000 people

Wasitthankasem R. et. al. PLOS ONE 2016

WHO TO TEST FOR CHRONIC HBV INFECTION

Testing approach and population	Recommendations*
General population testing	1. In settings with a ≥2% or ≥5% HBsAg seroprevalence in the general population, it is recommended that all adults have routine access to and be offered HBsAg serological testing with linkage to prevention, care and treatment services. General population testing approaches should make use of existing community- or health facility-based testing opportunities or programs such as at antenatal clinics, HIV or TB clinics. Conditional recommendation, low quality of evidence
Routine testing in pregnant women	2. In settings with a ≥2% or ≥5%% HBsAg seroprevalence in the general population, it is recommended that HBsAg serological testing be routinely offered to all pregnant women in antenatal clinics, with linkage to prevention, care and treatment services. Couples and partners in antenatal care settings should be offered HBV testing services. Strong recommendation, low quality of evidence
Focused testing in most affected populations	3. In all settings (and regardless of whether delivered through facility- or community- based testing), it is recommended that HBsAg serological testing and linkage to care and treatment services) be offered to the following individuals: • Adults and adolescents from populations most affected by HBV infection (i.e. who are either part of a population with high HBV seroprevalence or who have a history of exposures and/or high-risk behaviors for HBV infection); • Adults, adolescents and children with a clinical suspicion of chronic viral hepatitis (i.e. symptoms, signs, laboratory markers); • Sexual partners, children and other family members, and close household contacts of those with HBV infection; • Health-care workers: in all settings, it is recommended that HBsAg serological testing be offered and hepatitis B vaccination given to all health-care workers who have not been vaccinated previously (Adapted from existing guidance on Hepatitis B vaccination) Strong recommendation, low quality of evidence

WHO guidelines on HBV and HCV testing 2016



Adapt from Guidelines on hepatitis B and C testing. World Health Organization. Nov 2016

Specifications of available HBsAg rapid diagnostic tests

Test	Manufacturer	Nature of device	Matrices	Volume needed	Time to result	CE-marked	FDA-approved	WHO-prequalified
Determine™ HBsAg	Alere, Waltham, MA	Lateral flow	whole blood, serum, plasma	50 µl	15 min	No	No	No
VIKIA® HBsAg	bioMérieux, Marcy-l'Étoile, France	Lateral flow	Whole blood, serum, plasma	75 µl	15-30 min	Yes	No	No
DRW HBsAg rapid Test	Diagnostics for the Real World, San Jose, CA	Lateral flow	Serum, plasma	80 µl	30 min	Yes	No	No
Toyo HBsAg Rapid Test	Turklab, Izmir, Turkey	Flow-through	Whole blood, serum, plasma	100 µl	5-15 min	Yes	No	No
Assure HBsAg Rapid Test	MP Biomedicals, Singapore	Flow-through	Whole blood, serum, plasma	50 µl (whole blood) or 75µl (serum, plasma)	15-20 min	No	No	No
First Response HBsAg Card Test	Premier Medical Corporation, Daman, India	Flow-through	Serum, plasma	50 or 75µl	5-10 min	Yes	No	No
SD Bioline HBsAg	Standard Diagnostics, Yongin, Korea	Flow-through	Whole blood, serum, plasma	100 µl	20 min	No	No	No

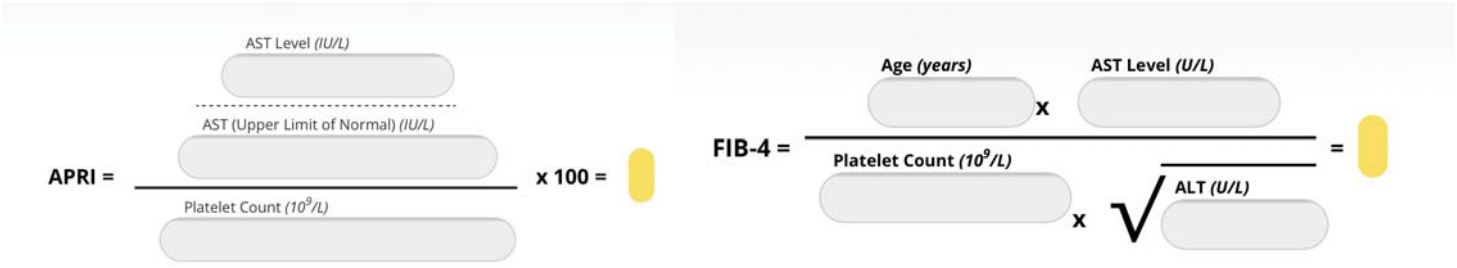
CE, European Conformity; FDA, US Food and Drug Administration; HBsAg, hepatitis B surface antigen; WHO, World Health Organization.

Chevaliez S. and Pawlotsky JM. J Hepatology 2018: 916-926.

Non-invasive assessment of liver disease severity

Test	Stage of fibrosis	Number of patients	Cut-off(s)	AUROC	Sensitivity	Specificity	PPV	NPV
FibroScan®	F3	560 HCV+	10 kPa*	0.83	72%	80%	62%	89%
	F4	1,855 HCV+	13 kPa*	0.90–0.93	72–77%	85–90%	42–56%	95–98%
ARFI (VTQ®)	F3	2,691 (1,428 HCV+)	1.60–2.17 m/sec	0.94 (0.91–0.95)‡	84% (80–88%)‡	90% (86–92%)‡	NA	NA
	F4	2,691 (1,428 HCV+)	2.19–2.67 m/sec	0.91 (0.89–0.94)‡	86% (80–91%)‡	84% (80–88%)‡	NA	NA
Aixplorer®	F3	379 HCV+	9 kPa*	0.91	90% (72–100%)‡	77% (78–92%)‡	NA	NA
	F4	379 HCV+	13 kPa*	0.93	86% (74–95%)‡	88% (72–98%)‡	NA	NA
FibroTest®	F4	1,579 (1,295 HCV+)	0.74	0.82–0.87	63–71%	81–84%	39–40	93–94
FIB-4	F4	2,297 HCV+	1–45† 3.25†	0.87§ (0.83–0.92)	90% 55%	58% 92%	NA	NA
APRI	F4	16,694 HCV+	1.0† 2.0†	0.84§ (0.54–0.97)	77% 48%	75% 94%	NA	NA

*Scales for liver stiffness cut-offs (in kPa) are different between FibroScan® and Aixplorer®;
†Two cut-offs are provided for FIB-4 and for APRI, respectively, with their own sensitivities and specificities;
‡95%CI; §Median (range)
EASL CPG HCV. J Hepatol 2018;69:461–511.



APRI score

> 0.7 had a sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis.
> 1.0 had a sensitivity of 76% and specificity of 72% for predicting cirrhosis
> 2.0 was more specific (91%) but less sensitive (46%)
> 0.5 the greater the negative predictive value and ability to rule out cirrhosis

Fib-4 score

<1.45 had a negative predictive value of 90% for advanced fibrosis
>3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis

Treatment indication for HBV

Significant virus that can trigger host immunologic response

+

Evidence of significant immune attack

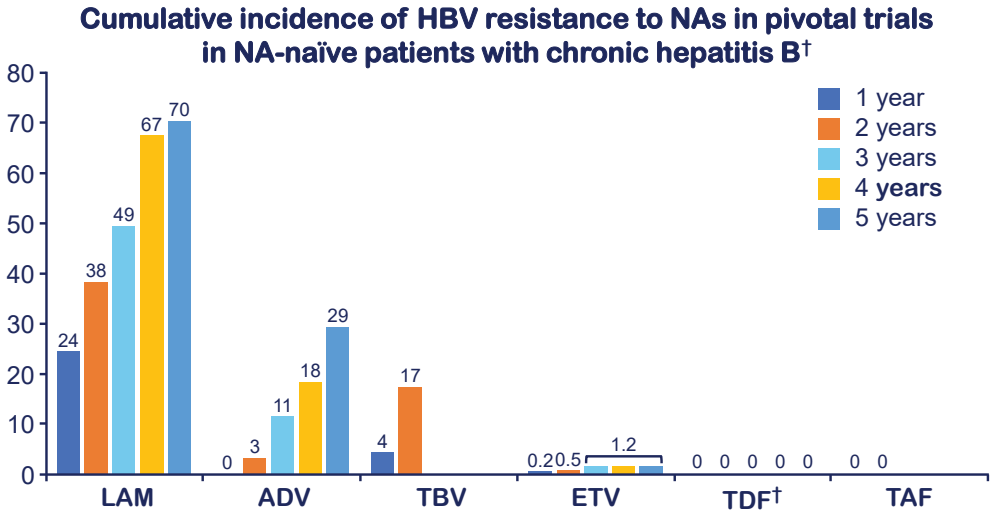
Inflammation (ALT) and/or Fibrosis

Anti-HBV Agents 2019

Agent	Route	Recommended Dose	
		Adult	Children
Peginterferon alfa-2a	SQ	180 µg/wk 48 wk	Not approved
Peginterferon alfa-2b	SQ	1.5µg/Kg/wk 48 wk	Not approved
Lamivudine#	PO	100 mg QD*	3 mg/kg/day (max: 100 mg/day)
Adefovir	PO	10 mg QD*	Not approved‡
Entecavir*	PO	▪ 0.5 mg QD (no previous LAM) ▪ 1.0 mg QD (if resists to LAM)*	Not approved
Telbivudine	PO	600 mg QD*	Not approved
Tenofovir*	PO	300 mg QD*	Not approved
Tenofovir Alafenamide	PO	25 mg QD**	Not approved

*Dose adjustment needed if eGFR < 50 mL/min. # Persons coinfected with HIV should receive 150 mg BID. Should only be used in combination with other antiretrovirals. ‡Approved for ages 12 and older. ** No dose adjustment needed if eGFR >15 mL/min

Prevention of resistance should rely on the use of first-line NAs with a high barrier to resistance*



*Evidence level I, grade of recommendation 1; †Collation of currently available data – not from head-to-head studies; ‡No evidence of resistance has been shown after 8 years of TDF treatment

EASL CPG HBV. J Hepatol 2017;67:370–98