HBsAg Positive and Thai Pilot Selection, Study of Royal Thai Air Force Population Model

Wg.Cdr.Roongaroon Thammalikhit MD

DIRECTOTATE OF MEDICAL SERVICES
ROYL THAI AIR FORCE

Disclaimer

“No conflict of interest exists in this study”

European Aviation Safety Agency

Annex to ED Decision 2011/015/R

(d) HIV infection

(1) HIV positivity is disqualifying. A fit assessment with a multi-pilot limitation may be considered for individuals with stable, non-progressive disease. Frequent review is required.

(2) The occurrence of AIDS or AIDS-related complex is disqualifying.

(e) Infectious hepatitis

Infectious hepatitis is disqualifying. A fit assessment may be considered after full recovery.

AMC1 MED.B.045 Obstetrics and gynaecology

Acute hepatitis B is grounding until liver enzymes return to normal.

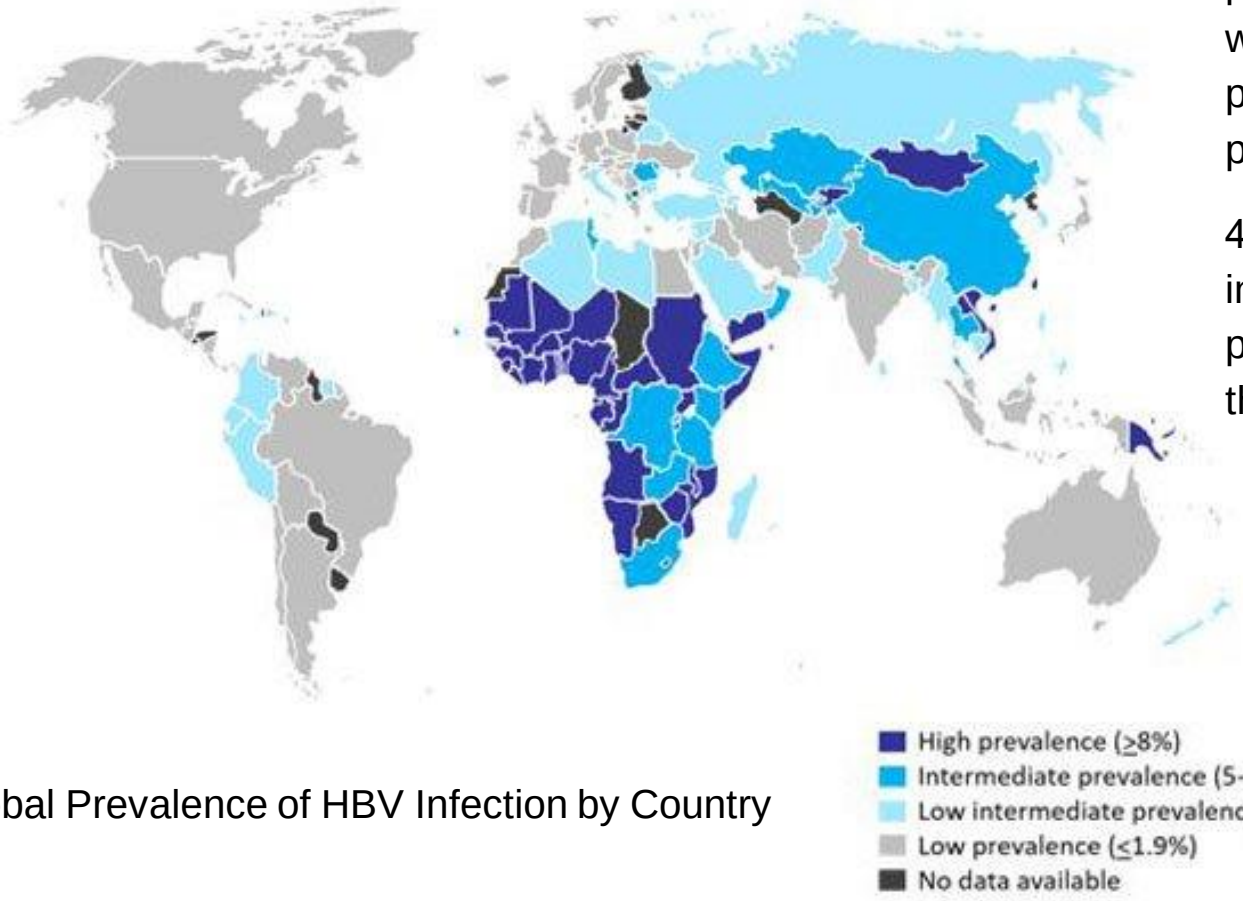
Chronic hepatitis B is disqualifying and requires a waiver. Any chronic hepatitis B infection that produces a symptomatic relapse is disqualifying and will not be waived.(In the US military,)

Clinical Practice Guideline for VIRAL HEPATITIS August 2, 2006
Aerospace Medical Association by their constituent organization American Society of Aerospace Medicine Specialists

civil aviation treatment with any form of Interferon alpha is disqualifying.

This is due to its side effect profile. Chronic hepatitis B may be qualifying, if it is stable.

Clinical Practice Guideline for VIRAL HEPATITIS August 2, 2006
Aerospace Medical Association by their constituent organization American Society of Aerospace Medicine Specialists



Global Prevalence of HBV Infection by Country

45% of the world population live in areas with a high CHB prevalence (≥8% of the population)

43% live in areas with intermediate CHB prevalence (2% to <8% of the population).[10]

In Thailand

HBsAg pooled prevalence estimate was 5.1%

HCC is the number one leading cancer of thai male population.

HbsAg related HCC is the main problem in Thailand .

Charline Leroi,Pierrick Adam,Woottichai Khamduang,Suttipong Kawilapat,Nicole Ngo-Giang-Huong,Sumet Ongwandee,Suchada Jiamsiri,Gonzague Jourdain International Journal of Infectious Diseases October 2016

non aviation RTAF population (ca.16000/year)
annual medical check up list are
CBC blood chemistry
chest radiograph
and urine examination.
RTAF population ab initio admission no HBsAg screening.

at division of Preventive Medicine Directorate of Medical Services

not included 12 Wing Air Force Bases outside Bangkok

since recent decades ,
all cadets from Military school,aircrew and aviation personnel will be screened HBsAg only at entrance process ,
if positive will be disqualified.

Medical Conditions for other Military recruitment in Thailand do not screen HBsAg .

medical check up and licensing of RTAF aircrew ,commercial air crews ATC and aviation personel (ca.5000+14,000/ year) at Institute of Aviation Medicine RTAF

Chronic hepatitis is a more significant aeromedical problem. fatigue and malaise, affecting safety of flight,indefinite amount of time. progress to chronic liver disease, cirrhosis, or hepatocellular carcinoma.

Clinical Practice Guideline for VIRAL HEPATITIS. American Society of Aerospace Medicine Specialists August 2, 2006

EASA AMC Med B.0.35:

Infectious Hepatitis is disqualifying. A fit assessment may be considered after full recovery.

Hepatitis B

Acute hepatitis B is disqualifying. Certification may be considered upon full recovery (viral clearance).

Acceptable Means of Compliance and Guidance Material to Part-MED1 European Aviation Safety Agency 15 December 2011

EASA AMC Med B.0.35: Infectious Hepatitis is disqualifying. A fit assessment may be considered after full recovery.

Chronic hepatitis B – Certification may be considered in pilots in the immune tolerant' or inactive HBV carrier state.

Pilots are required to submit a report from a liver specialist, to include:

- History of infection Current symptoms
- Stability of condition Liver Function Tests
- HBV serology HBV DNA levels
- Alpha-foetoprotein (AFP) Report of ultrasound of the liver.

Requirement for treatment is disqualifying.

Acceptable Means of Compliance and Guidance Material to Part-MED1 European Aviation Safety Agency 15 December 2011

2018 FAA

GUIDE FOR AVIATION MEDICAL EXAMINERS

II. Examination Techniques

1. Observation: The Examiner should note any unusual shape or contour, skin color, moisture, temperature, and presence of scars. Hernias, hemorrhoids, and fissure should be noted and recorded.

   A history of acute gastrointestinal disorders is usually not disqualifying once recovery is achieved, e.g., acute appendicitis.

   Many chronic gastrointestinal diseases may preclude issuance of a medical certificate (e.g., cirrhosis, chronic hepatitis, malignancy, ulcerative colitis). Colostomy following surgery for cancer may be allowed by the FAA with special followup reports.

   The Examiner should not issue a medical certificate if the applicant has a recent history of bleeding ulcers or hemorrhagic colitis. Otherwise, ulcers must not have been active within the past 3 months.

III. Aerospace Medical Disposition

The following is a table that lists the most common conditions of aeromedical significance, and course of action that should be taken by the examiner as defined by the protocol and disposition in the table. Medical certificates must not be issued to an applicant with medical conditions that require deferral, or for any condition not listed in the table that may result in sudden or subtle incapacitation without consulting the AMCD or the RFS. Medical documentation must be submitted for any condition in order to support an issuance of an airman medical certificate.

DISEASE/CONDITION	CLASS	EVALUATION DATA	DISPOSITION
Abdomen and Viscera and Anus Conditions			
Cholelithiasis	All	Document history and findings	If asymptomatic – Issue Otherwise - Requires FAA Decision
Cirrhosis (Alcoholic)	All	See Substance Abuse/Dependence Disposition in Item 47.	Requires FAA Decision
Cirrhosis (Non-Alcoholic)	All	Submit all pertinent medical records, current status report, to include history of encephalopathy; PT/PTT; albumin; liver enzymes; bilirubin; CBC; and other testing deemed necessary	Requires FAA Decision
Colitis	All	Submit all pertinent	Follow the CACI – Colitis

๒.๓.๒.๗ ผลที่ตามมาจากโรคหรือจากการผ่าตัดในช่องท้อง (Sequelae of disease or surgical intervention) ซึ่งอาจเป็นสาเหตุให้เกิดการพร่องสมรรถภาพขณะทำหน้าที่ เช่น การอุดตัน ตีบแคบ หรือกดทับของทางเดินอาหาร ให้ถือว่า “ไม่สมบูรณ์”

๒.๓.๒.๘ ผู้ร้องขอที่ได้รับการผ่าตัดใหญ่ในช่องท้องที่ต้องตัดทางเดินอาหารออกไปทั้งหมดหรือส่วนหนึ่งส่วนใด รวมทั้งอวัยวะอื่น ๆ ภายในช่องท้องด้วย ให้ถือว่า “ไม่สมบูรณ์” อย่างน้อย ๓ เดือน หลังจากนั้นเมื่อผลของการผ่าตัดแสดงว่าจะไม่กระทบกระเทือนต่อความปลอดภัยในการปฏิบัติหน้าที่จึงถือว่า “สมบูรณ์” ตามผนวก ๕ ข้อ ๕.๔.๔

๒.๓.๒.๙ ผู้ร้องขอที่มีอาการของตับอักเสบไม่ว่าชนิดใดหรือการตรวจพบว่าอยู่ในระยะแพร่กระจายโรคได้ ให้ถือว่า “ไม่สมบูรณ์” หากได้รับการรักษาและไม่มีอาการหรือพบว่ามีภูมิคุ้มกัน (Antibody) ให้ถือว่า “สมบูรณ์” ให้ประเมินผลตามคำแนะนำในผนวก ๕ ข้อ ๕.๔.๖

ข้อ ๒.๔ มาตรฐานระบบเมตาโบลิซึม โภชนาการและโรคของระบบต่อมไร้ท่อ (Metabolic, Nutritional and Endocrine disease)

any symptomatic hepatitis of any type in infectious stage is disqualified,after treatment with asymptomatic or with immunity (antibody) will be qualified.

CAAT

สำนักงานการบินพลเรือนแห่งประเทศไทย

The Civil Aviation Authority of Thailand

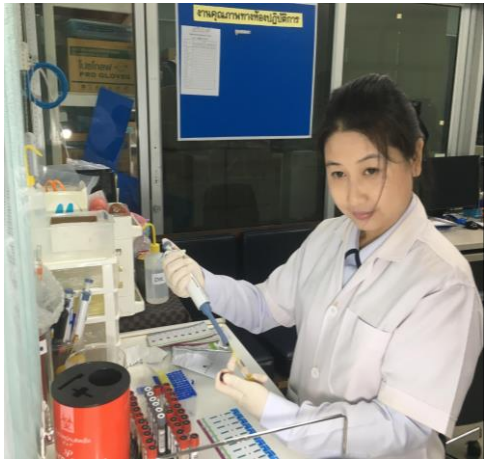
cirrhosis and hepatocellular carcinoma will lose pilot license permanently with financial compensated by insurance - company

Selection of main airlines commercial pilot in thailand are qualified without HBsAg positive with MOU for few decades.

Material and Method

- Population : RTAF personnel
  annual medical check up

- Prospective cohort study
  from 1 November 2016 to 31 October 2017
  screening with HBsAg test repeat to confirm
  with HBsAg and antiHBcAb
  HBsAg quantitative test
- Age 20 to 60 years of age
- Gender both male and female



HBsAg test brand certified
by immunochromatography assay
high sensitivity and specificity
95 and 100%,
positive and negative predictive
values were 100 and 99.7%,
respectively.

A rapid immunochromatographic assay for hepatitis B virus screening.

Lemon SM, Doo E, Ghany MG, Miskovsky E, Woods GL, Park Y, Hoofnagle JH. J Viral Hepat. 2003 Jul;10(4):331-4.Lau DT1, Ma H,

Excluded :

- false positive HBsAg
- pre existing Hepatocellular Carcinoma
- preexisting treatment of HBV hepatitis
- anti HCV positive
- excessive alcohol drinking
- alcohol dependent

Initial data include

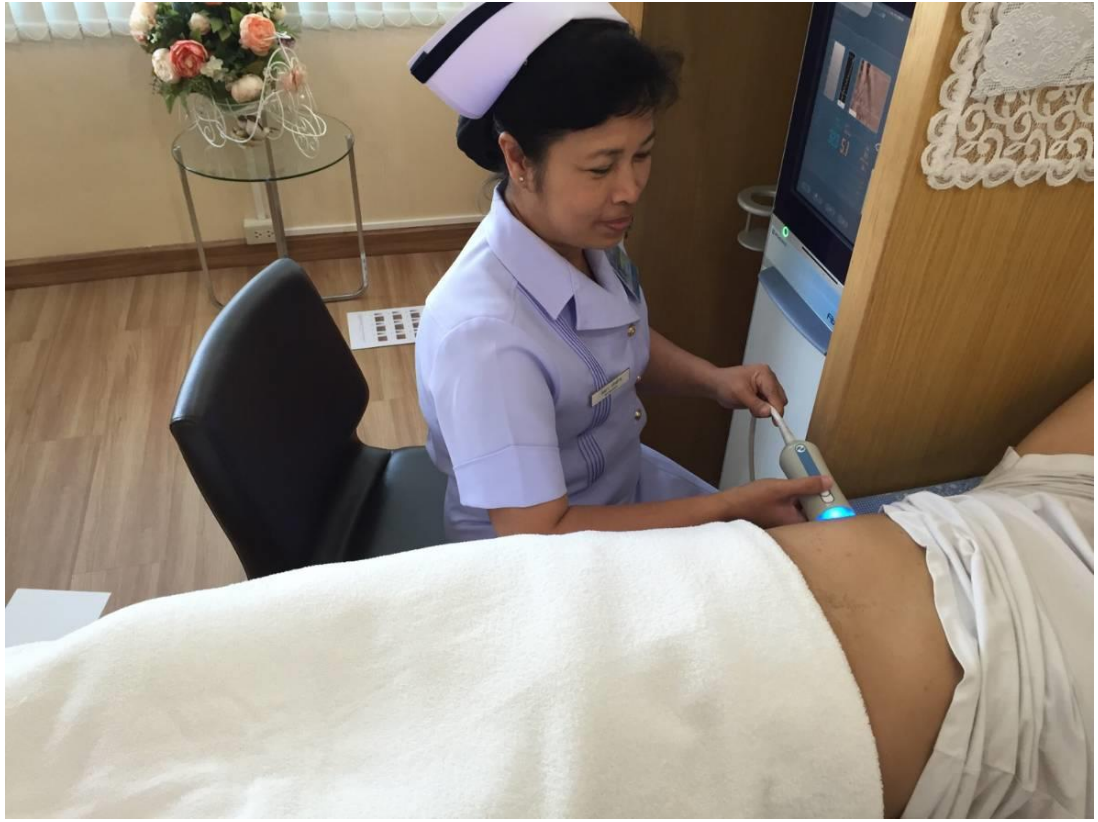
1 personal history : age gender HT BW
family history history of HBV test or treatment
smoking alcohol personal disease etc.

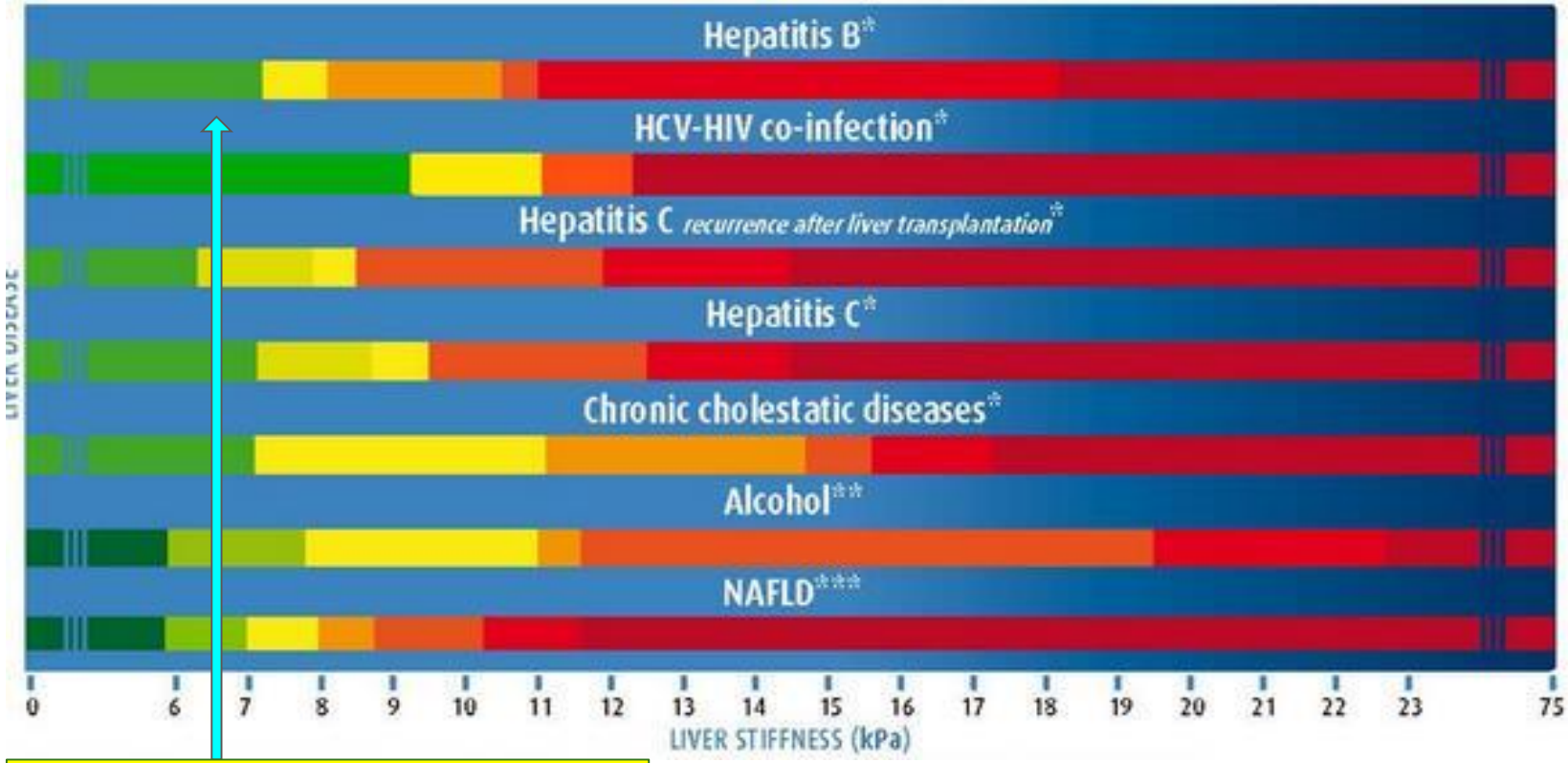
2 blood test : blood chemistry CBC
HBsAg HBsAg quantitative
anti HCV HBV DNA HBeAg antiHBcAb

3 fibroscan

4 ultrasonogram of upper abdomen

fibroscan for hepatic elasticity





fibroscan > 6.5

Several HCC risk scores based on risk factors such as cirrhosis, age, male gender, and high viral load have been used, and have optimal negative predictive values of ≥ 95%.
Most of these have been derived from, and internally validated in, treatment-naïve Asian CHB patients.

Prediction models of hepatocellular carcinoma development in chronic hepatitis B patients, Hye Won Lee and Sang Hoon Ahn World J Gastroenterol. 2016 Oct 7; 22(37): 8314–8321.

HCC prediction models,

including IPM (Individual Prediction Model) score,
CU-HCC (Chinese University-HCC) score,
GAG-HCC (Guide with Age, Gender, HBV DNA, Core Promoter Mutations and Cirrhosis-HCC) score, NGM-HCC (Nomogram-HCC) score,
REACH-B (Risk Estimation for Hepatocellular Carcinoma in Chronic Hepatitis B) score,
and Page-B score.

Prediction models of hepatocellular carcinoma development in chronic hepatitis B patients, Hye Won Lee and Sang Hoon Ahn World J Gastroenterol. 2016 Oct 7; 22(37): 8314–8321.

Accurate prediction of HCC risk is important for decisions on antiviral therapy and HCC surveillance.

The REACH-B score a community cohort of non-cirrhotic, better applied in the primary care setting.

Can we use HCC risk scores to individualize surveillance in chronic hepatitis B infection? J Hepatol. 2015 Sep; 63(3):722-32.Wong VW, Janssen HL.

The GAG-HCC and CU-HCC scores were derived from hospital cohorts and include cirrhosis as a major integral component. more applicable to patients at specialist clinics, the diagnosis of cirrhosis based on routine imaging and clinical parameters can be inaccurate.

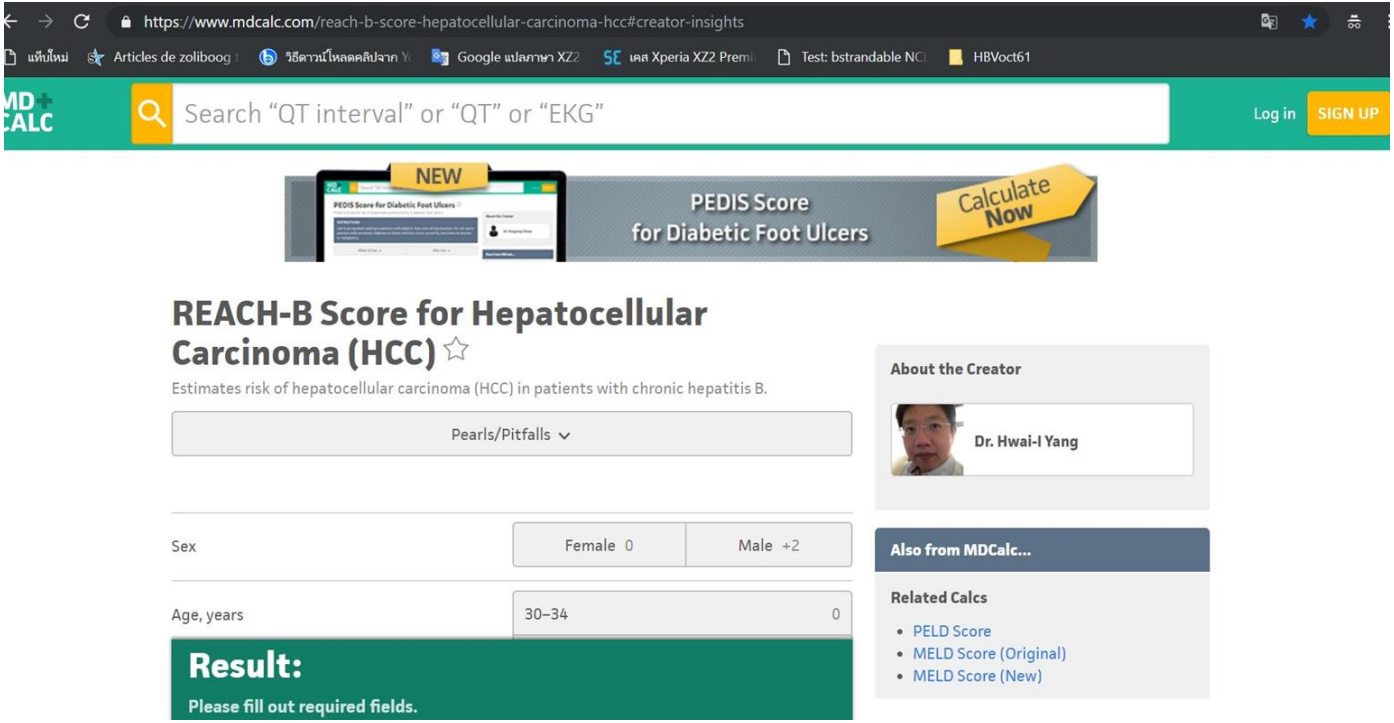
Can we use HCC risk scores to individualize surveillance in chronic hepatitis B infection? J Hepatol. 2015 Sep;63(3):722-32. doi: 10.1016/j.jhep.2015.05.019. Epub 2015 May 27.

REACH-B Score for Hepatocellular Carcinoma (HCC)

Estimates risk of hepatocellular carcinoma (HCC) in patients with chronic hepatitis B non cirrhotic.

in liver stiffness measurement (LSM) using transient elastography to predict HCC.LSM-HCC score constructed from LSM, age, serum albumin and HBV DNA level is accurate to predict HCC in CHB patients.

https://www.mdcalc.com/reach-b-score-hepatocellular-carcinoma-hcc#creator-insights



12 points

REACH-B Score

13.4 %

10-year risk of HCC (See 3-year and 5-year risk in the Evidence section)

Copy Results | Next Steps

» Next Steps | Evidence | Creator Insights

Interpretation:

REACH-B Score	HCC risk		
	3-year	5-year	10-year
0	0.0%	0.0%	0.0%
1	0.0%	0.0%	0.1%
2	0.0%	0.0%	0.1%
3	0.0%	0.1%	0.2%
4	0.0%	0.1%	0.3%
5	0.1%	0.2%	0.5%
6	0.1%	0.3%	0.7%
7	0.2%	0.5%	1.2%
8	0.3%	0.8%	2.0%
9	0.5%	1.2%	3.2%
10	0.9%	2.0%	5.2%
11	1.4%	3.3%	8.4%
12	2.3%	5.3%	13.4%

the **1 percent rule** risk threshold that is applied to the medical fitness of pilots. The "1 percent rule" states that a 1% per annum risk of medical incapacitation is the threshold between acceptable and unacceptable.

Watson, Dougal B. (January 2005). "Aeromedical decision-making: an evidence-based risk management paradigm". Aviation, Space, and Environmental Medicine. 76 (1): 58–62. PMID 15672988.

EASL 2017
management of hepatitis B virus infection
European Association for the Study of the Liver

Clinical Practice Guidelines

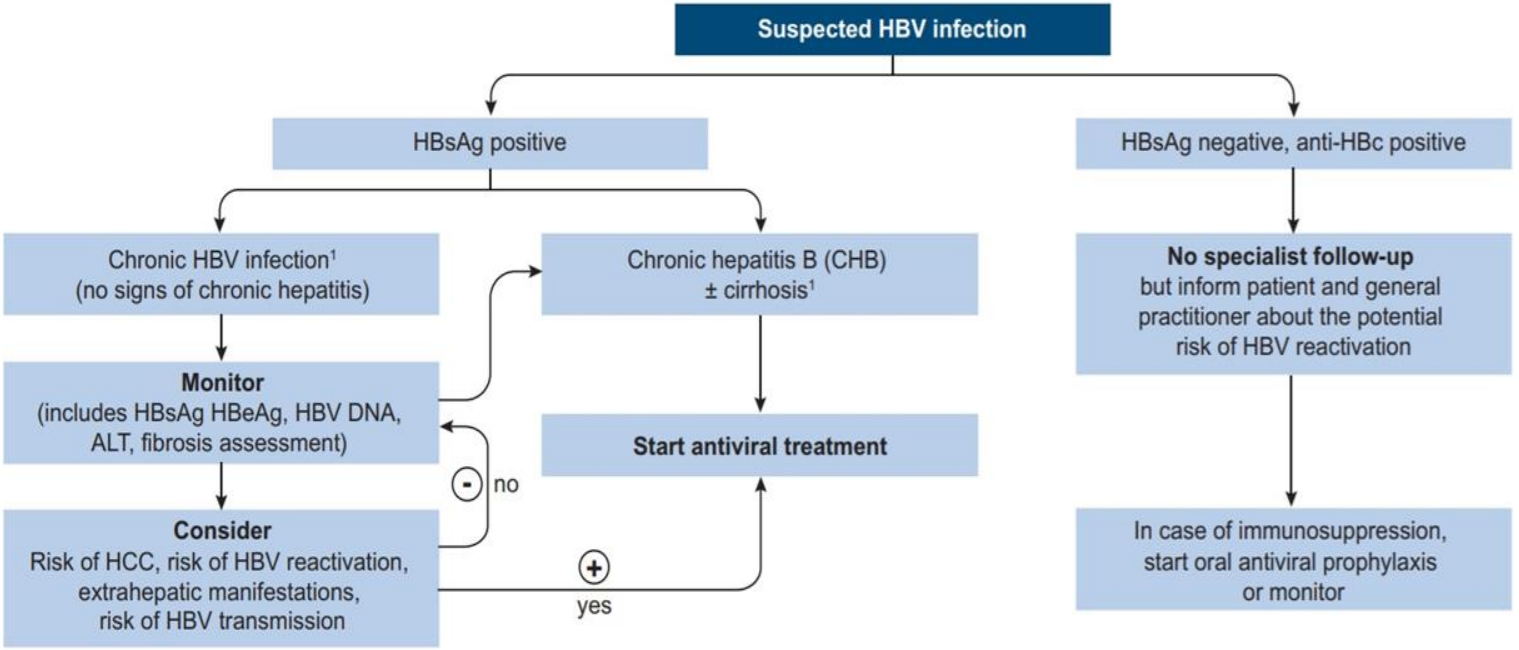


Fig. 2. Algorithm for the management of HBV infection. [1]see definitions in text and Fig. 1.

แนวทางการดูแลรักษาผู้ป่วยไวรัสตับอักเสบ
บี และ ซี เรื้อรังในประเทศไทย ปี 2558

Thailand Practice Guideline for Management of Chronic Hepatitis B and C 2015

in Thailand family history is very strong indicator of HCC risk but the magnitude of the risk has not been well studied.

First-degree relatives of patients with HCC have a 2-fold increase in HCC incidence.

The effect of family history appears to be synergistic to HBV carriage.

1 Synergistic effects of family history of hepatocellular carcinoma and hepatitis B virus infection on risk for incident hepatocellular carcinoma. Loomba R et al. Clin Gastroenterol Hepatol 2013 Dec; 11:1636. 2 Family History Is Important in Assessing HCC Risk in Chronic HBV Infection Atif Zaman, MD, MPH Associate Editor NEJM JOURNAL WATCH GASTROENTEROLOGY January 13, 2014

grouping by risk factors

1 male age > 40 female > 50.

2 family history of HCC or CLD

3 significant hepatic fibrosis 1/4 of

- 3.1 physical examination cirrhotic stigmata
- 3.2 fibroscan >5.9
- 3.3 U/S inhomogeneous parechyma to cirrhotic pictures
- 3.4 fibrotest > F2

4 history of chronic hepatitis > 6 months

- SGOT > 37 U/L
- SGPT > 42 U/L

5 HBV-DNA level > 2000 IU/mL

6 HBeAg positive

→ gp I
0-1 number

→ gp II
not I and III

→ gp III
> or= 3
numbers

group I only follow up HCC surveillence.

group II should have follow up until fullfill indication criteria of treatment.

group III active group : definitely must treat according to guideline more than 3 in 5.

RESULT

Result 1

Total 15436 cases of RTAF population

77.25% male 22.75% female

Abnormal transaminase enzyme 1711 cases

HBsAg positive 611 case

or 3.96 % of prevalence rate.

15436 cases

HBsAg positive

611

60 %complete work up

366

male 122/309
female 10/59

fibro > 6.5
132 cases

Active Diease gp

> 10 reach B
scores 31 cases

fibro < 6.5
183 cases

3 cases of
advanced cancer

schemic flow chart of risk ranking

male from over 40 years of age 5 % prevalence

ratio of HBsAg positive/total number 611/15436 (3.96%)		
age (years)	number of male gp (%)	number of female gp (%)
21-30	77/3190 (2.4)	14/1017 (1.3)
31-40	95/2252 (4.2)	27/933 (2.8)
41-50	154/2853 (5.3)	9/501 (1.7)
51-60	186/3586 (5.1)	39/1054 (3.7)
all age group	512/11925 (4.3)	99/3511 (2.8)

Result 2

minimum prevalence rate in each age group in male from over 40 years of age are almost 5 %. Under 40 years of age prevalence rate is increase with age.

In female prevalence rate increase by age getting older prevalence is higher.

Result 3

Naive HBsAg positive with complete study and follow up evaluation 366 cases. advanced asymptomatic Hepatocellular Carcinoma (HCC) in this screening was positive 2 cases

or minimum prevalence rate of 546 per 100,000 persons.

HCC 305 /100000* Thai population

- * Hepatocellular carcinoma screening and surveillance in 2293 chronic hepatitis B patients in an endemic area. World J Gastroenterol. 2016 Sep 14; 22(34): 7806–7812.Tawesak Tanwandee, and Chirayu U Auewarakul

Result 4

Naive HBsAg positive with complete study

and follow up evaluation 366 cases.

advanced asymptomatic Cholangio Carcinoma Carcinoma (CCA)

in this screening was positive 1 case

minimum prevalence rate 1/15463*100000

RTAF minimum prevalence = 6.48/100000

national prevalence CCA 5.5 / 100000 **

- ** National and Subnational Population-Based Incidence of Cancer in Thailand: Assessing Cancers with the Highest Burdens Shama Virani , Surichai Bilheem , Wasan Chansaard , Imjai Chitapanarux 4 ID , et al cancers 2017, 9, 108

2 asymtomatic advanced HCC +1 CCA

male 36 years old → SR 6 mo
two TACE embolization
and HCC ruptured massive bleedding
hepatic failure

male 58 years old → SR 4 mo
Targeted therapy:
with Tyrosine
kinase inhibitors
Sorafenip
lung metas. +hepatic
failure

CCA
male 57
years old → SR 9 mo
partial hepatectomy
and hepatic failure 4 mo. P/O

all pass away
4-9 mo after DX

2 asymtomatic advanced HCC + 1 CCA

SR 6 mo
two TACE embolisation
ruptured HCC and
massive bleeding hepatic
failure BX

SR 4 mo
Targeted therapy:
with sorafenip
Tyrosine kinase
inhibitors
lung metas +hepatic
failure BX

SR 9 mo
partial hepatectomy
and hepatic failure 4 mo. P/O

Although annually checkup every year without hepatitis B test,HCC and cirrhosis may be not detected in every age group.

Result 5

Active viral replication
with HBeAg positive
or HBV DNA > 170,000,000 IU/mL
total 54 cases

Result 6

Both gender

age gp 21-30 years old 62/366 16.94 %

HBeAg positive or higher viral load 22/62

high risk in gp III 36/62

age gp 31-40 years old 81/366 22.13 %

HBeAg positive or higher viral load 14/81

high risk in gp III 44/81

Result 6

Both gender

age gp 41-50 years old 93/366 25.40 %

HBeAg positive or higher viral load 11/93

high risk in gp III 68/93

age gp 51-60 years old 128/366

HBeAg positive or higher viral load 7/128

high risk in gp III 85/128

	group 1		group 2		group 3		total	
years old	number	% group I	number	% group II	number	% group III	total number	%
20 to 30	1	0.27	25	6.83	36	**9.84**	62	16.94
31 to 40	0	0	37	10.11	44	**12.02**	81	22.13
41 to 50	0	0	25	6.83	68	**18.58**	93	25.41
51 to 60	0	0	44	12.02	86	**23.50**	130	35.52
	1	**0.27%**	**131**	**35.79%**	**234**	**63.93%**	**366**	**100.00%**

more than half both gender in high risk

total 366 cases	% gender	%HBeAg	% group I	% group II	% group III
male	84.43	15.86	0.3	34.0	**65.7**
female	15.57	8.77	0	45.60	**54.38**

Discussion and conclusion

HBsAg positive male RTAF population 63.96 % in high risk group III require urgent or immediate therapeutic intervention to prevent long term complications.

HBsAg positive in RTAF population without significant hepatic fibrosis have at least 16.94 % with opportunities to develop HCC in 3 to 5 years more than 1 % without therapeutic option.

Lower prevalence rate 2.4% in (21-30 years old) younger age group after national whole country expanded vaccination program implementation in 1992 compare to over 4-5 % in male older age group.

Hepatitis B seroprevalence in Thailand: 12 years after hepatitis B vaccine integration into the national expanded programme on immunization.Chongsrisawat V1, et al Trop Med Int Health. 2006 Oct;11(10) :1496-502.

The REACH-B score derived from a community cohort of non-cirrhotic patients and is better applied in the aviation setting with high sensitivity and may be lower specificity.

Can we use HCC risk scores to individualize surveillance in chronic hepatitis B infection? Journal of Hepatology Volume 63, Issue 3, September 2015, Pages 722-732 Vincent Wai-SunWong Harry L.A. Janssen

other various HCC predictor models, derived from hospital cohorts and include cirrhosis as a major integral component may be more applicable to patients at specialist clinics.

Can we use HCC risk scores to individualize surveillance in chronic hepatitis B infection? Journal of Hepatology Volume 63, Issue 3, September 2015, Pages 722-732 Vincent Wai-SunWong Harry L.A. Janssen

Overall, these scores have high negative predictive values of over 95% in excluding HCC development in 3 to10 years.

Can we use HCC risk scores to individualize surveillance in chronic hepatitis B infection? Journal of Hepatology Volume 63, Issue 3, September 2015, Pages 722-732 Vincent Wai-SunWong Harry L.A. Janssen

Engaging aircrews with CHB in the continuum of care.

Most of infected individuals are asymptomatic until the development of cirrhosis or HCC.

In developed country, only 30% of infected individuals are aware of their diagnosis, and only a small fraction of these individuals are linked to care .

Due to delayed diagnosis until the development of cirrhosis or HCC, the morbidity and mortality risks are greatly increased.

Therefore, identification of infected individuals early in their disease is critical.

Appropriate risk group should be fully investigated and treatment until viral and clinical are well controlled.

This study may provide some informations for AME to monitor the treatment and progression of disease.

aircrew with HBsAg positive

1 identify active group and high risk group
FH age gender transminase AFP HBV-DNA HBeAg HBsAg quatitative and signify stage of hepatic fibrosis

2 use appropiate HCC risk score models to assess each check up

3 obesity and diabetes also have higher risk of HCC . by the increased fibrosis progression and lesser response of fibrosis regression after Rx .

4 treatment regimen with interferon is disqualified

5 entecavir and tenofovir are better effective and less side effects,may be considered without limitation.

Risk Factors for the Development of Hepatocellular Carcinoma in Thailand. Taned Chitapanarux*,1 and Kannika Phornphutkul1,2 J Clin Transl Hepatol. 2015 Sep 28; 3(3): 182–188.

Conclusion (1)

With out screening and interval control with optimal test in naive HBsAg carrier or chronic hepatitis B have chance to develop HCC or cirrhotic complications.

Conclusion(2)

Thai commercial pilots or aircrews ATC and other aviation personnel in older age group (at least more than 50 years old) should have HBsAg screening and identified of risk factors.

Thank you