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

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ROYL THAI AIR FORCE
Disclaimer

“No conflict of interest exists in this study”
(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,)
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.
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 Ongwande, 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 personnel (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.
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
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.

<table>
<thead>
<tr>
<th>DISEASE/CONDITION</th>
<th>CLASS</th>
<th>EVALUATION DATA</th>
<th>DISPOSITION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abdomen and Viscera and Anus Conditions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholelithiasis</td>
<td>All</td>
<td>Document history and findings</td>
<td>If asymptomatic – Issue FAA Decision</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Otherwise - Requires FAA Decision</td>
</tr>
<tr>
<td>Cirrhosis (Alcoholic)</td>
<td>All</td>
<td>See Substance Abuse/Dependence Disposition in Item 47</td>
<td>Requires FAA Decision</td>
</tr>
<tr>
<td>Cirrhosis (Non-Alcoholic)</td>
<td>All</td>
<td>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</td>
<td>Requires FAA Decision</td>
</tr>
<tr>
<td>Colitis</td>
<td>All</td>
<td>Submit all pertinent medical records</td>
<td>Follow the CACI – Colitis</td>
</tr>
</tbody>
</table>
any symptomatic hepatitis of any type in infectious stage is disqualified, after treatment with asymptomatic or with immunity (antibody) will be qualified.
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.
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.

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.
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.

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.
REACH-B Score for Hepatocellular Carcinoma (HCC)

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

Pearls/Pitfalls

Sex
- Female 0
- Male +2

Age, years
- 30–34
- 0

Result:
Please fill out required fields.
### REACH-B Score Interpretation:

<table>
<thead>
<tr>
<th>REACH-B Score</th>
<th>HCC risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3-year</td>
</tr>
<tr>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>1</td>
<td>0.0%</td>
</tr>
<tr>
<td>2</td>
<td>0.0%</td>
</tr>
<tr>
<td>3</td>
<td>0.0%</td>
</tr>
<tr>
<td>4</td>
<td>0.0%</td>
</tr>
<tr>
<td>5</td>
<td>0.1%</td>
</tr>
<tr>
<td>6</td>
<td>0.1%</td>
</tr>
<tr>
<td>7</td>
<td>0.2%</td>
</tr>
<tr>
<td>8</td>
<td>0.3%</td>
</tr>
<tr>
<td>9</td>
<td>0.5%</td>
</tr>
<tr>
<td>10</td>
<td>0.9%</td>
</tr>
<tr>
<td>11</td>
<td>1.4%</td>
</tr>
<tr>
<td>12</td>
<td>2.3%</td>
</tr>
</tbody>
</table>
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.

Clinical Practice Guidelines

Suspected HBV infection

HBsAg positive

Chronic HBV infection¹ (no signs of chronic hepatitis)

Monitor (includes HBsAg HBeAg, HBV DNA, ALT, fibrosis assessment)

Consider
Risk of HCC, risk of HBV reactivation, extrahepatic manifestations, risk of HBV transmission

Chronic hepatitis B (CHB) ± cirrhosis¹

Start antiviral treatment

HBsAg negative, anti-HBc positive

No specialist follow-up but inform patient and general practitioner about the potential risk of HBV reactivation

In case of immunosuppression, start oral antiviral prophylaxis or monitor

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

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
group I only follow up HCC surveillance.

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
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

60% complete work up

611 cases

366 cases

fibro > 6.5
132 cases

male 122/309
female 10/59

fibro < 6.5
183 cases

> 10 reach B
scores 31 cases

Active Disease gp

3 cases of advanced cancer

schematic flow chart of risk ranking
male from over 40 years of age 5 % prevalence

<table>
<thead>
<tr>
<th>age (years)</th>
<th>number of male gp (%)</th>
<th>number of female gp (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-30</td>
<td>77/3190 (2.4)</td>
<td>14/1017 (1.3)</td>
</tr>
<tr>
<td>31-40</td>
<td>95/2252 (4.2)</td>
<td>27/933 (2.8)</td>
</tr>
<tr>
<td>41-50</td>
<td>154/2853 (5.3)</td>
<td>9/501 (1.7)</td>
</tr>
<tr>
<td>51-60</td>
<td>186/3586 (5.1)</td>
<td>39/1054 (3.7)</td>
</tr>
<tr>
<td>all age group</td>
<td>512/11925 (4.3)</td>
<td>99/3511 (2.8)</td>
</tr>
</tbody>
</table>

ratio of HBsAg positive/total number 611/15436 (3.96%)
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

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  \[ \frac{1}{15463} \times 100000 \]

RTAF minimum prevalence  = 6.48/100000

national prevalence CCA 5.5 / 100000 **

2 asymptomatic advanced HCC +1 CCA

male 36 years old

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

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 asymptomatic 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.
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
<table>
<thead>
<tr>
<th>years old</th>
<th>group 1</th>
<th></th>
<th>group 2</th>
<th></th>
<th>group 3</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number</td>
<td>%</td>
<td>number</td>
<td>%</td>
<td>number</td>
<td>%</td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>20 to 30</td>
<td>1</td>
<td>0.27</td>
<td>25</td>
<td>6.83</td>
<td>36</td>
<td>9.84</td>
</tr>
<tr>
<td>31 to 40</td>
<td>0</td>
<td>0</td>
<td>37</td>
<td>10.11</td>
<td>44</td>
<td>12.02</td>
</tr>
<tr>
<td>41 to 50</td>
<td>0</td>
<td>0</td>
<td>25</td>
<td>6.83</td>
<td>68</td>
<td>18.58</td>
</tr>
<tr>
<td>51 to 60</td>
<td>0</td>
<td>0</td>
<td>44</td>
<td>12.02</td>
<td>86</td>
<td>23.50</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0.27%</td>
<td>131</td>
<td>35.79%</td>
<td>234</td>
<td>63.93%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>366</td>
<td>100.00%</td>
</tr>
</tbody>
</table>
more than half both gender in high risk

<table>
<thead>
<tr>
<th>total 366 cases</th>
<th>% gender</th>
<th>%HBeAg</th>
<th>% group I</th>
<th>% group II</th>
<th>% group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>male</td>
<td>84.43</td>
<td>15.86</td>
<td>0.3</td>
<td>34.0</td>
<td>65.7</td>
</tr>
<tr>
<td>female</td>
<td>15.57</td>
<td>8.77</td>
<td>0</td>
<td>45.60</td>
<td>54.38</td>
</tr>
</tbody>
</table>
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.

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.

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.
Overall, these scores have high negative predictive values of over 95% in excluding HCC development in 3 to 10 years.
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
   quantitative and signify stage of hepatic fibrosis
2 use appropriate 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.

Conclusion (1)
Without 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