

Bible Class: Hepatitis B Virus Infection

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What is the HBV prevalence?

Hepatitis B

- Worldwide approx. 350 Mio. chronically infected with HBV
- Approx. 40% of the world population: anti-HBc-Antibodies positive
- Approx. 15 Mio. chronically HBV infected in Europe
- Switzerland 0.3-0.5% (24000)
- Worldwide annually, 0,6 -1 Mio. people die from complications of chronic HBV-Infection (WHO, 2002)
- HBV responsible for 60% of all HCC cases worldwide

What are Hepatitis B Risk Factors?

Hepatitis B Risk Factors

- Blood contamination
 - IV-Drug Abuse
 - Injured mucus membranes
- Sexual Transmission
- Perinatal Transmission



What is the new nomenclature for HBV

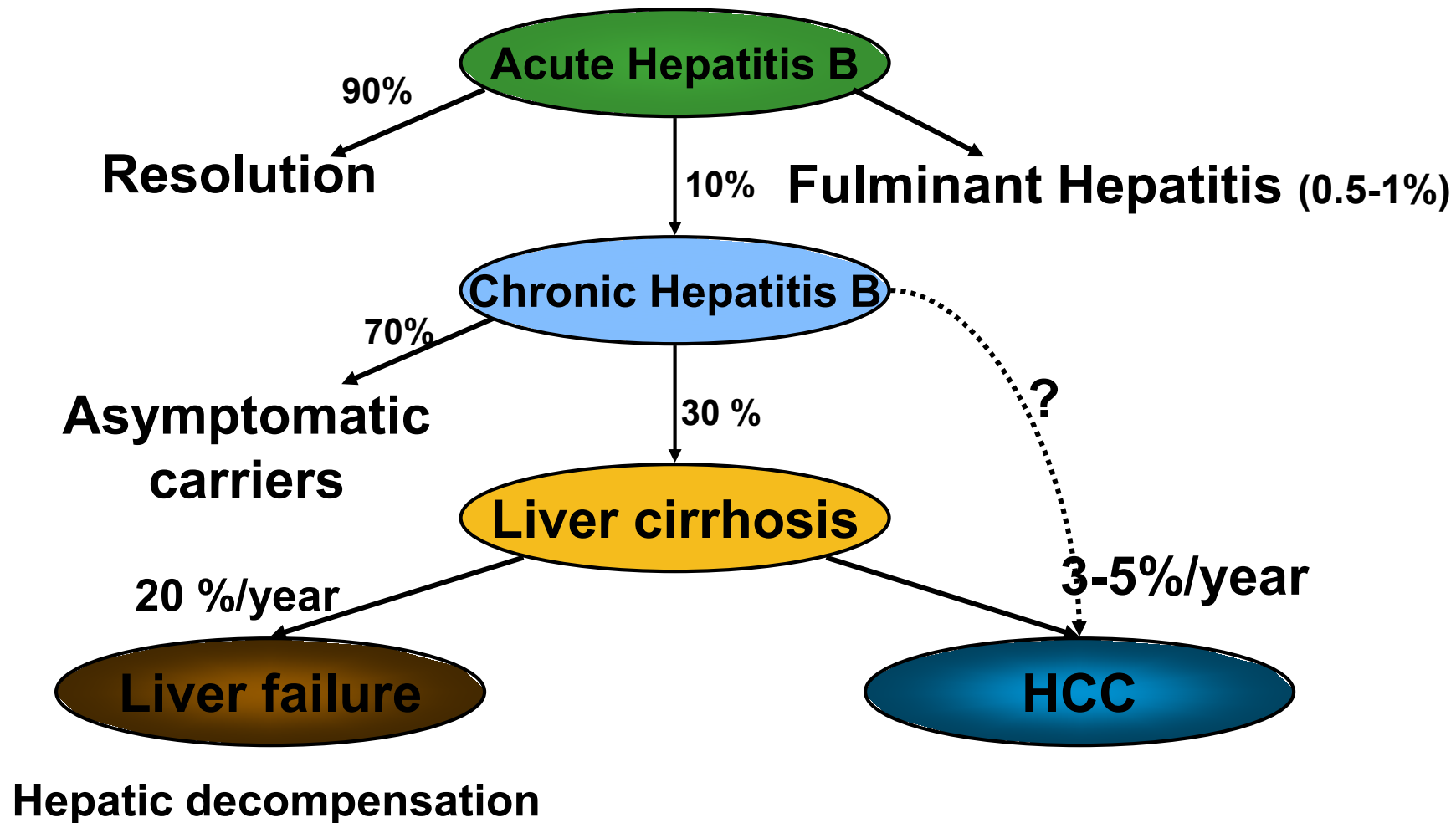
New nomenclature for HBV

	HBeAg positive		HBeAg negative	
	Chronic infection	Chronic hepatitis	Chronic infection	Chronic hepatitis
HBsAg	High	High/intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	>10 ⁷ IU/ml	10 ⁴ -10 ⁷ IU/ml	<2,000 IU/ml ^{oo}	>2,000 IU/ml
ALT	Normal	Elevated	Normal	Elevated*
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative chronic hepatitis

Fig. 1. Natural history and assessment of patients with chronic HBV infection based upon HBV and liver disease markers. *Persistently or intermittently. ^{oo}HBV DNA levels can be between 2,000 and 20,000 IU/ml in some patients without signs of chronic hepatitis.

Natural course of HBV Infection?

Natural Course of Hepatitis B Infection



Who to screen for HBV ?

Hepatitis B

Whom to screen?

- Elevated Liver enzymes and/or signs of hepatitis or chronic liver disease of unknown origin
- Liver cirrhosis/-fibrosis
- New diagnosis of HCC
- Pat. with migration background and from regions with high HBsAg prevalence (Africa, East Europe, Mediterranean)
- Family member or sexual partner from HBV infected patients

Hepatitis B

Whom to screen?

- Medical staff
- Homosexuals a/o persons with frequent changing sexual partners
- Active o. previous i.v.-drug abuse
- Dialysis patients

Hepatitis B

Whom to screen?

- HIV- a/o HCV-infected Pat.
- Recipients of organs before transplantation
- Blood- and Organ donors
- Patients before or during immunosuppressive therapy or Chemotherapy
- Pregnant women (HBsAg)

Hepatitis B

How to screen?

Hepatitis B Screening

How?

	HBsAg	Anti-HBc	Anti-HBs	HBV DNA
Chron. HBV	+	+	-	+/-
Acute HBV	+	IgM +	-	+
Elimin. HBV	-	+	+	(-)
HBV Vaccine	-	-	+	(-)

HBeAg, Anti-HBe

Prevention of HBV Reactivation??

Algorithm??

Risk of Hepatitis B Reactivation Associated With Immunosuppressive Therapies

Risikogruppe	Medikamente/Serologie	Risiko der Reaktivierung	Evidenzgrad
Hohes Risiko: >10%	B cell-depletierende Medikamente: <i>Rituximab/Ofatumumab</i> HBsAg pos/anti-HBc pos HBsAg neg/anti-HBc pos	30%–60% >10%	A A
	Anthrazykline z.B. <i>Doxorubicin</i> HBsAg pos/anti-HBc pos	15-30%	B
	Steroide >4 Wo >20 mg HBsAg pos/anti-HBc pos	>10%	B
Moderates Risiko: 1–10%	TNF-α-Inhibitoren: <i>Infliximab, Adalimumab, Etanercept</i> Andere Cytokin-Inhibitoren Tyrosinkinase-Inhibitoren HBsAg pos & anti-HBc pos HBsAg neg & anti-HBc pos	1%–10% 1%	B/C C
Moderates Risiko: 1–10%	Steroide >4 Wo 10–20 mg HBsAg neg & anti-HBc pos	1%–10%	C
	Steroide >4 Wo <10 mg HBsAg pos & anti-HBc pos	1%–10%	C
	Anthratzykline z.B. <i>Doxorubicin</i> HBsAg neg/anti-HBc pos	1%–10%	C
Low risk: <1%	Azathioprin, Methotrexat <i>6-Mercaptopurin</i> HBsAg pos & anti-HBc pos HBsAg neg & anti-HBc pos Intrartikuläre Steroide oder Steroide <1 Wo per os in jeder Dosierung Steroide >4 Wochen <10mg per os HBsAg pos & anti-HBc pos HBsAg neg & anti-HBc pos	<1% <<1% <1% <<1%	A A A/B A/B

Prevention of HBV reactivation in immunosuppression

HBsAg +



Prophylactic antiviral Tx
(NUCs) for up to 12-18 months after
end of immunosuppr. Tx
Liver function + HBV DNA every 3
to 6 months

**HBsAg -
Anti-HBc +**

High/moderate risk

Low risk

Monitor HBV DNA/HBsAg
Q1-3 months
if DNA/HBsAg pos.
→ NUCs

**HBsAg -
Anti-HBc -
Anti-HBs -**



Vaccination

Before start of immuno-
suppressive Tx

When to treat pregnant HBV pos. women?

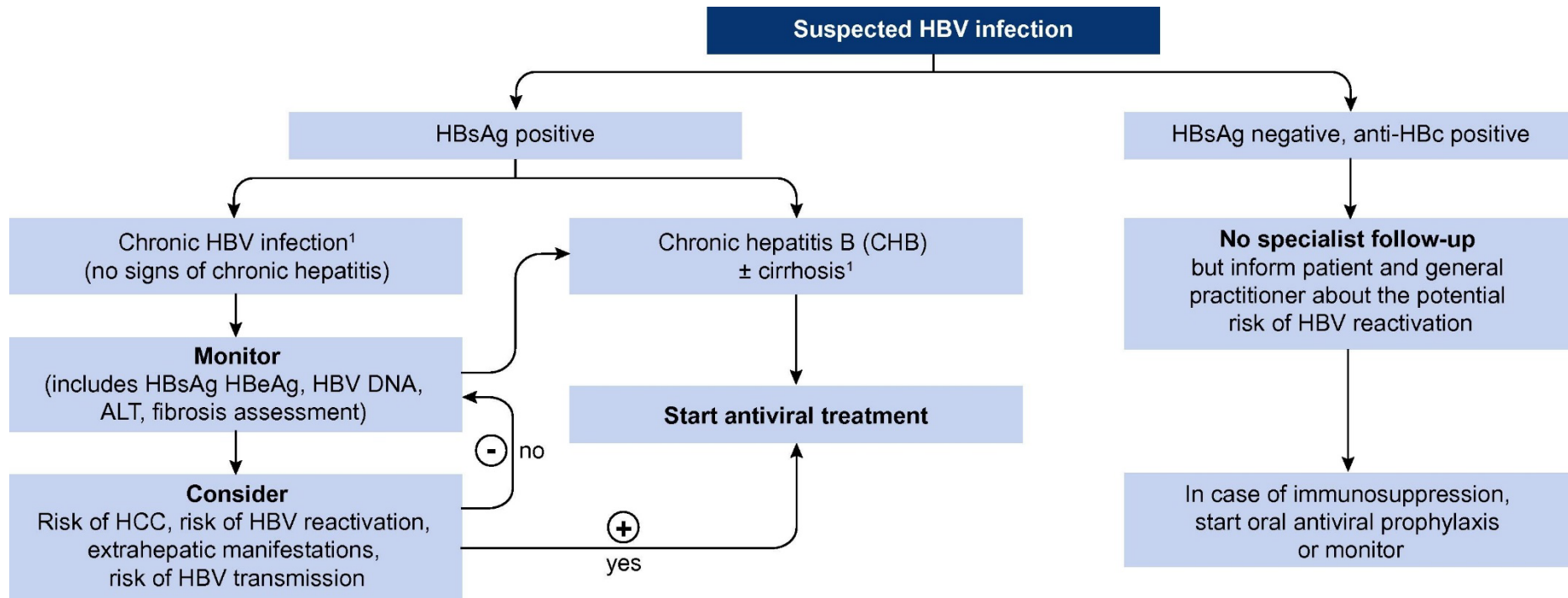
Vertical transmission despite active and passive vaccination

- N=1068 children from HBeAg positive mothers
- 3% vertical Transmission with HBV DNA $>10^6$ cop/ml
- 5,5 % vertical Transmission with HBV DNA $>10^7$ cop/ml
- 9,6% vertical Transmission with HBV DNA $>10^8$ cop/ml


→ Antiviral Therapy in 2./3. Trimester with HBV-VL >200.000 IU/ml until 12 W postpartal

When to treat HBV ?

HBV Treatment Indication



Natural history of HBV and treatment indications



PHASE	1	2	3	4
New terminology	HBeAg positive Chronic <u>infection</u>	HBeAg positive Chronic <u>hepatitis</u>	HBeAg negative Chronic <u>infection</u>	HBeAg negative Chronic <u>hepatitis</u>
Old terminology	<i>Immune tolerant</i>	<i>HBeAg-positive CHB</i>	<i>Inactive carrier</i>	<i>HBeAg-negative CHB</i>
HBsAg	High	High/Intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	>10E7 IU/mL	10E4-10E7 IU/mL	<2,000 IU/mL*	>2,000 IU/mL
ALT	Normal	Elevated	Normal	Elevated**
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Disease progression	Low	Moderate to high	No, very low	Moderate to high
Treatment	Not indicated***	Indicated	Not indicated	Indicated

* HBV-DNA levels can be between 2,000 and 20,000 IU/mL in some patients without signs of chronic hepatitis

** Persistently or intermittently; *** Treatment is indicated in some patients

How to treat HBV?

HBV- Treatment: HOW?

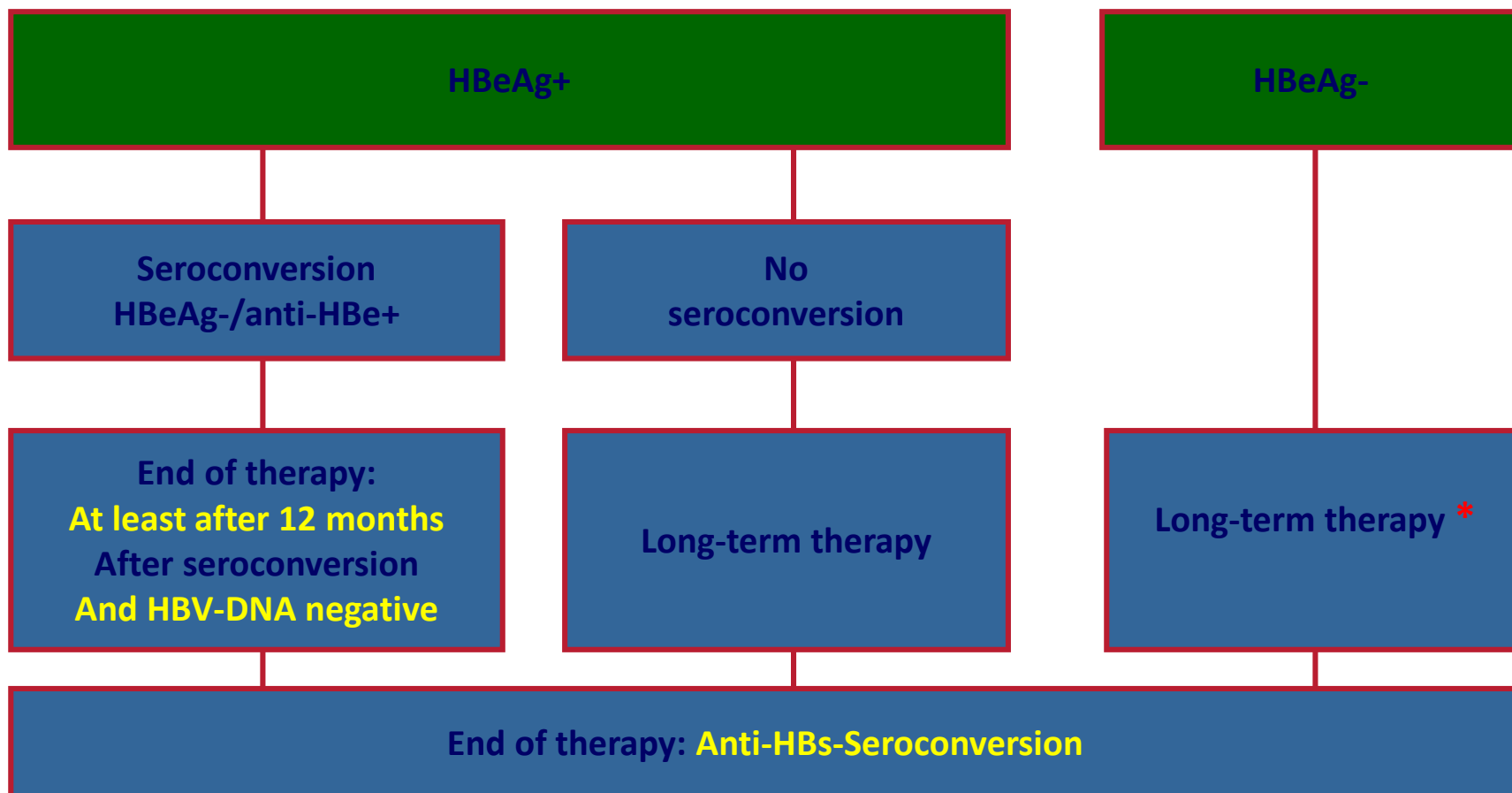
NUCs

TDF/TAF or ETV

Can NUCs be stopped?

When to stop NUC therapy ?

Treatment End points



Algorithm for stopping NUCs in HBeAg-negative patients

HBeAg neg CHB – NA Therapy

Viral suppression

Cirrhosis

Post-treatment monitoring

yes

no

yes

no

Continue NA

HBsAg levels < 100 - 500 IU/mL

Continue NA

yes

no

Stop NA
and monitor

Continue NA

THANK YOU