



VHPB TECHNICAL MEETING

Long term hepatitis B vaccination and treatment

29-30 March 2022

Response to the hepatitis B vaccine and influence of sex, age of vaccination and time from the third dose. Meaning of the antibody value below 10 IU/L.

Andrea Trevisan, Chiara Bertoncello, Marco Fonzo

*Department of Cardiac Thoracic Vascular Sciences and Public Health
University of Padova*

MAIN QUESTIONS

- 1. MANDAROTY OR NOT**
- 2. AGE OF VACCINATION**
- 3. SEX**
- 4. PROTECTIVE ANTIBODIES**
- 5. INTERVAL**

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Table 1. HBV vaccination survey in some European countries according to age of first vaccine dose and in relation to the modality of implementation.

Country	Age of first dose	Implementation
Belgium	2 months	Recommended*
Bulgaria	At birth	Mandatory
Cyprus	2 months	Recommended
Czech Republic	3 months	Mandatory
Estonia	At birth	Recommended
France	2 months	Recommended†
Germany	2 months	Recommended
Hungary	At birth	Mandatory
Ireland	2 months	Recommended
Italy	3 months	Mandatory
Latvia	At birth	Mandatory
Lithuania	At birth	Recommended
Luxembourg	2 months	Recommended
Malta	15 months	Recommended
Poland	At birth	Mandatory
Portugal	At birth	Recommended
Romania	At birth	Mandatory
Slovakia	2 months	Mandatory
Slovenia	Before school	Mandatory
Spain	2 months	Recommended

Denmark, Finland, Iceland, The Netherlands, Norway, Sweden and UK have a selective immunization program for at-risk subjects.
 *Mandatory for at-risk subjects only.
 The data are derived from [6] and [7].

Table 2. Recommendation for HBV vaccination for healthcare workers in some European countries.

Country	Implementation
Austria	Recommended
Belgium	Mandatory
Czech Republic	Mandatory
Denmark	Recommended ^a
France	Mandatory
Germany	Recommended
Ireland	Recommended
Italy	Recommended
Luxembourg	Recommended
Netherlands	Recommended
Norway	Recommended ^b
Poland	Mandatory
Slovenia	Mandatory
Spain	Recommended
Sweden	Recommended
Switzerland	Recommended
UK	Recommended

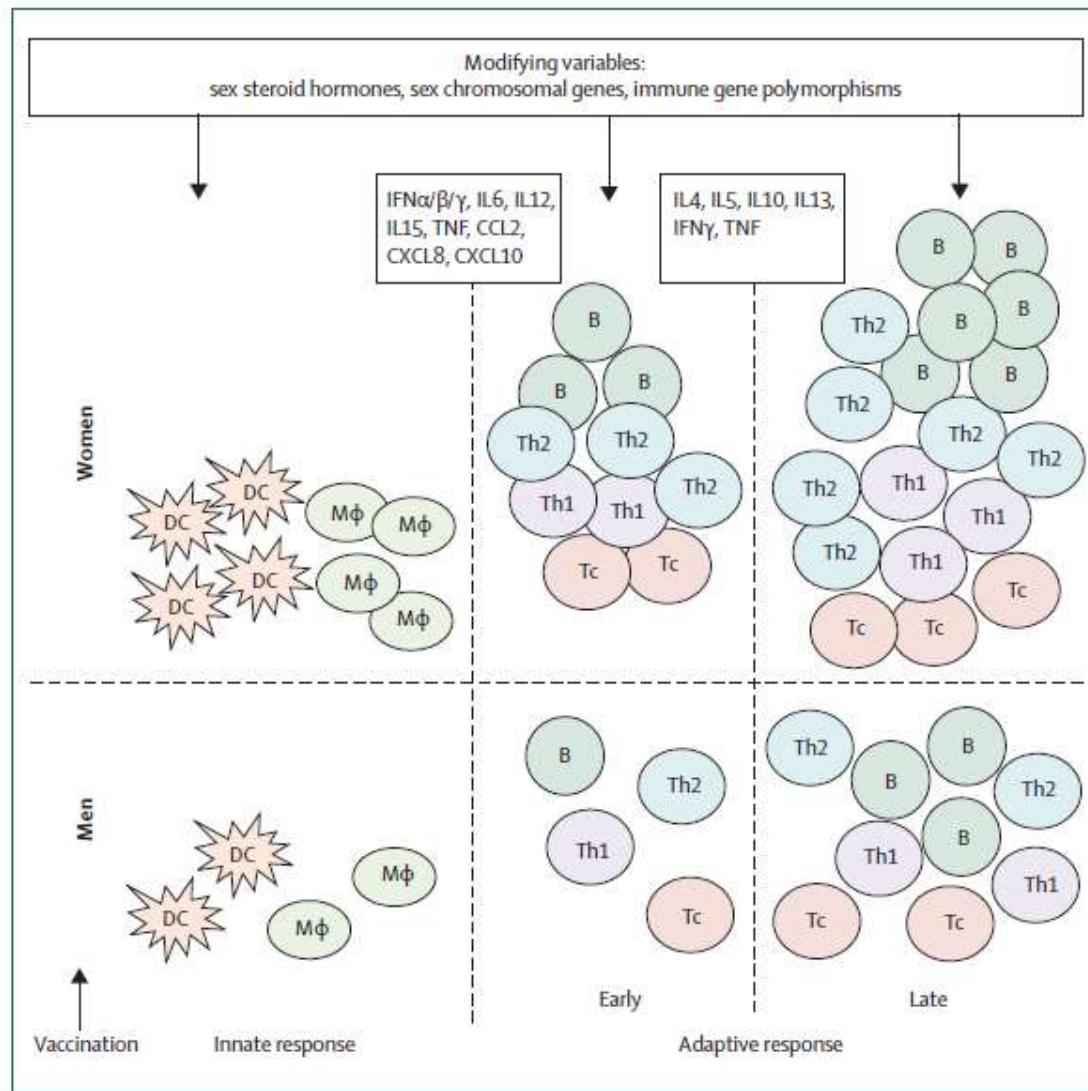
^aOnly for medical and nursing staff.

^bOnly for medical, nursing, and paramedical staff and for medical students.

The data are derived from [74].

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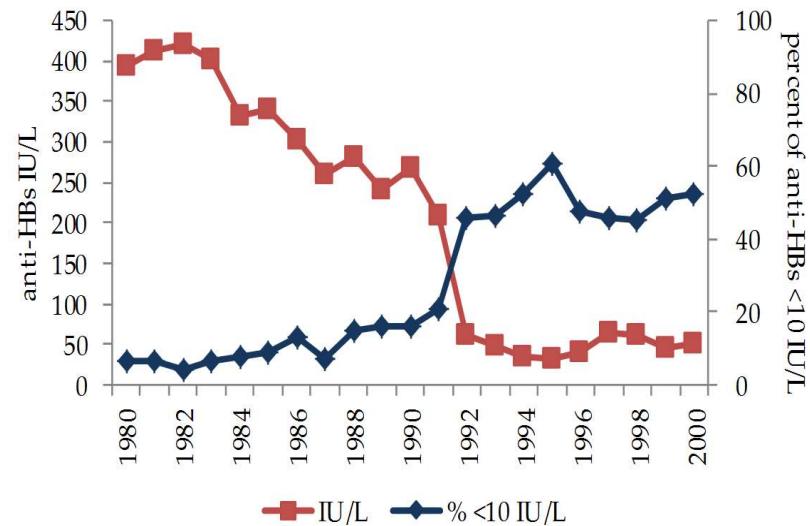
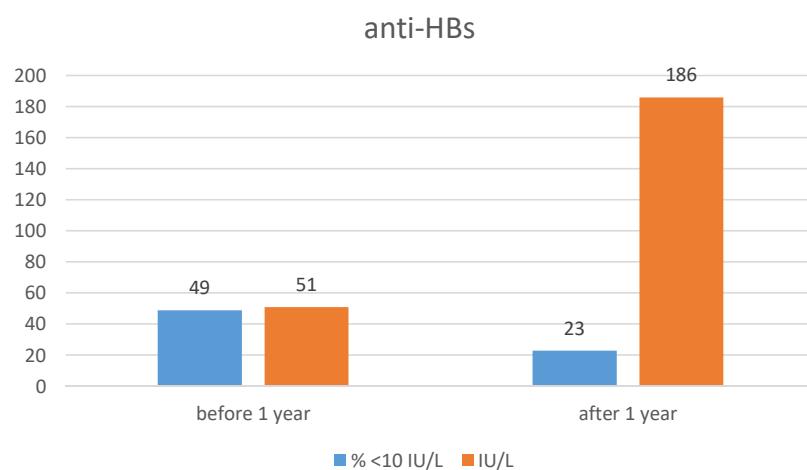
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Klein et al, 2010

	N.	<10 IU/L	%	χ^2	p	titre IU/L	p	time days	time years
before	6013	3017	50.2			50.1 ± 127.9		7076.2 ± 383.9	19.4 ± 1.1
after	383	62	16.2	165.235	<0.0001	222.0 ± 314.7	<0.0001	6717.8 ± 686.4	18.4 ± 1.9

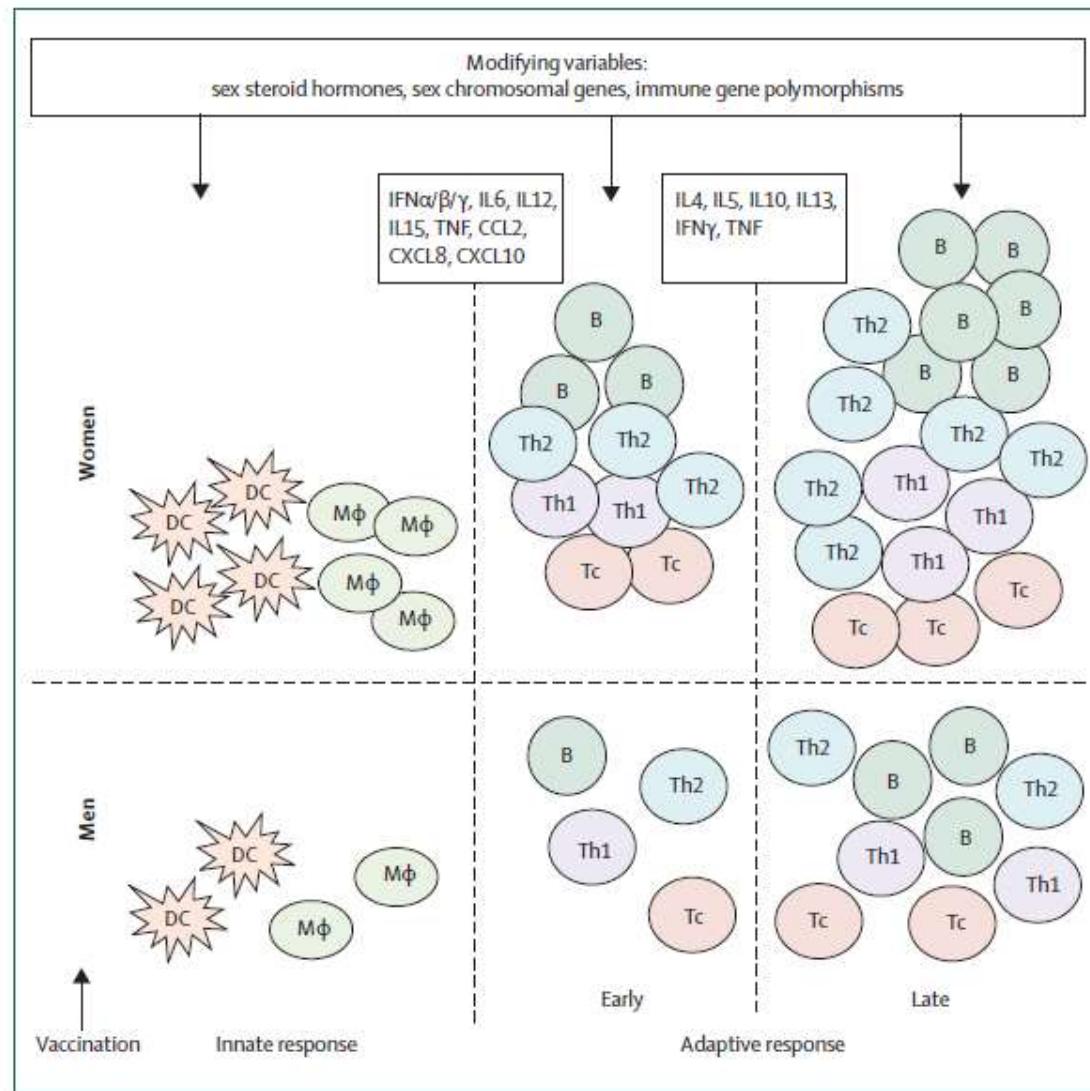
Trevisan et al. Hum Vaccin Immunother 16 460-464 2020



Trevisan et al Int J Environ Res Public Health 18 7783 2021

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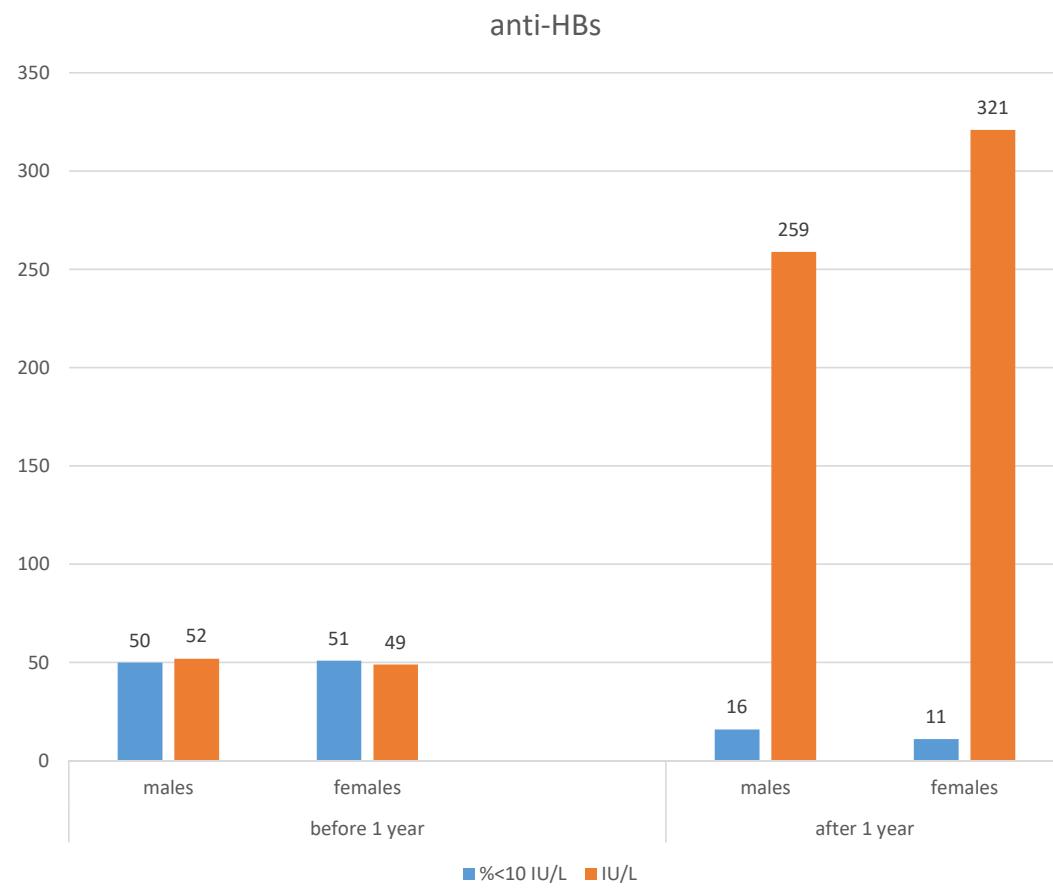
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Klein et al, 2010

	B	R	t	P
Intercept	639.633055		3.917674	= 0.0001
Age	-0.268772	-0.051849	-1.602757	= 0.1093
Sex	62.683428	0.089948	2.788052	= 0.0054
pre-booster markers	77.556552	0.493004	17.492981	< 0.0001
age 1st dose	0.244005	0.048039	1.48471	= 0.138
interval 3rd dose/analysis	0.230044	0.04476	1.383148	= 0.1669
interval booster/analysis	-1.342746	-0.154398	-4.824238	< 0.0001

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part b (to achieve)	10 IU/L	100 IU/L	1000 IU/L
all (pre-booster marker)	0.76	1.08	4.32
males (pre-booster marker)	1.05	1.33	4.12
females (pre-booster marker)	0.58	0.94	4.54

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		post-booster							
pre-booster	No.	anti-HBs levels							
IU/L		0.00-9.99	%	10-99	%	100-1000	%	>1000	%
0.00-0.09	108	35	32.4	34	31.5	36	33.3	3	2.8
0.10-0.99	321	33	10.3	120	37.4	146	45.5	22	6.9
1.00-1.99	254	9	3.5	46	18.1	150	59.1	49	19.3
2.00-9.99	347	5	1.4	34	9.8	135	38.9	173	49.9
all	1030	82	8.0	234	22.7	467	45.3	247	24.0

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All Students	b	r	t	p
Intercept	101.326457		23.188326	<0.0001
year of birth	-0.049739	-0.208528	-22.548445	<0.0001
sex	0.031555	0.017194	1.818617	=0.069
time	-0.000152	-0.228768	-24.852321	<0.0001

Vaccinated before 1 year of age	b	r	t	p
Intercept	-34.537893		-3.868822	<0.0001
year of birth	0.017517	0.050819	3.944496	<0.0001
sex	-0.035231	-0.019884	-1.541681	=0.1232
time	0.000086	0.036904	2.862629	=0.0042

Vaccinated after 1 year of age	b	r	t	p
Intercept	110.800937		13.20865	<0.0001
year of birth	-0.054679	-0.17756	-12.974467	<0.0001
sex	0.148749	0.079279	5.718946	<0.0001
time	-0.000075	-0.092701	-6.694957	<0.0001

interval years	anti-HBs
0	385.5
5	345.7
10	305.9
15	272.7
20	226.4
25	193.8
30	146.8
35	107.0
40	67.2
45	27.4
47.2	10.0
47.9	4.0
48.2	2.0
48.3	1.0
50	0.0

SUGGESTIONS AND CONCLUSIONS

1. if the vaccine is not done immediately at birth to avoid infection from HBsAg positive mothers (but just evaluate the maternal serology) it makes no sense to establish a vaccination schedule at three months preferring to move the vaccine after one year of age (especially in countries with low endemicity);
2. consider 2 IU/L the "so-called" non-protective value because at this value of anti-HBs the response to the booster dose is always optimal; this avoids additional expense for both booster doses and antibody control after the booster dose.
3. since adaptive immunity begins (around one year of age) the response to the HBV vaccine (as for others) is linked to sex (generally females respond more and more readily);
4. this difference in response is not evident whether the vaccine is given at birth or at three months of age.

Thanks for your
attention