Technical Viral Hepatitis Prevention Board meeting
Milan, Italy, November 17-18, 2011

Hepatitis B vaccination: a completed schedule … enough to control HBV lifelong?

Breakthrough HBV infections in vaccinated people: a ten-year surveillance study in Italy

November 18th, 2011

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What is a breakthrough infection?

A breakthrough infection is an infection caused by the live virus in a vaccinated individual

breakthrough infection refers to:

- ✓ **an infection resulting in serological test positive for HBV**
- ✓ **and/or clinical disease**

SEIEVA is able to give information on clinical cases

SEIEVA data on hepatitis B vaccination

Section of SEIEVA epidemiological questionnaire

22	Was you given at least one dose of **hepatitis B vaccine**?	1 Yes, 1 dose 0 No 8 not known 2 Yes, 2 doses 3 Yes, 3 doses
22.a	If Yes: 1° dose - vaccine type _____ date	*dd* |__|__| *mm* |__|__| *yy* |__|__|
22.b	2° dose - vaccine type _____ date	*dd* |__|__| *mm* |__|__| *yy* |__|__|
22.c	3° dose - vaccine type _____ date	*dd* |__|__| *mm* |__|__| *yy* |__|__|

SEIEVA 2001-2010

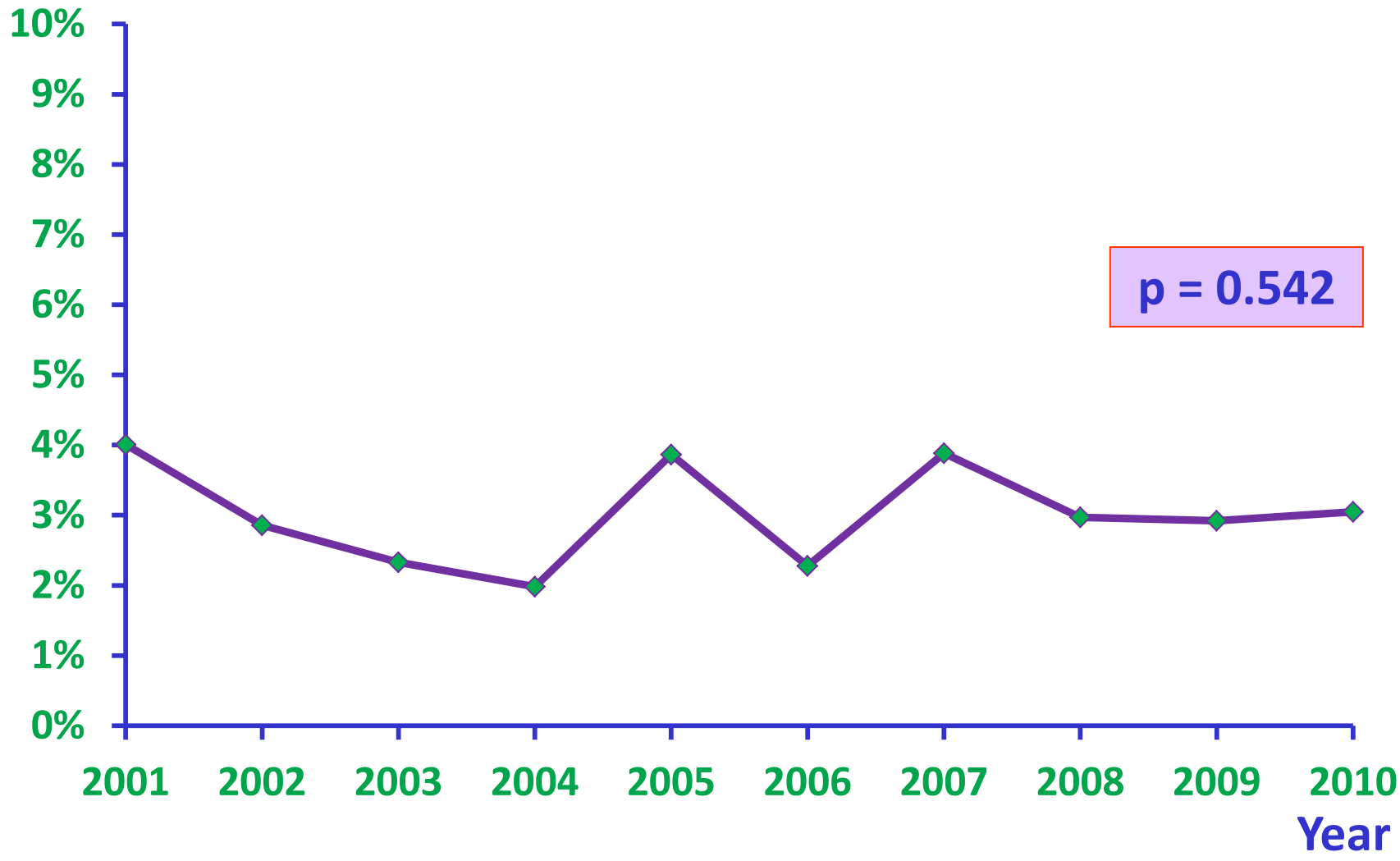
4,773 out of 5,252 hepatitis B cases notified to SEIEVA (90.9%) had filled in the information on hepatitis B vaccination

Distribution of hepatitis B cases by vaccination

Study of possible breakthrough infections

Hepatitis B vaccination	n°	%
yes	144	3.0
no	4,629	97.0
Total	4,773	100.0

Percentage of vaccinated people among acute hepatitis B cases, by year



Distribution of acute hepatitis B cases in vaccinees by gender, age and vaccination status

Gender	Hepatitis B vaccination yes		Hepatitis B vaccination no		p value
M	94	65.7%	3,498	76.2%	0.004
F	49	34.3%	1,094	23.8%	
Total	143	100.0%	4,592	100.0%	

	Hepatitis B vaccination yes	Hepatitis B vaccination no	p value
Age			
Mean (SD)	35.9 (14.7)	41.0 (14.0)	<0.001

Risk factors associated to hepatitis B cases among vaccinated and unvaccinated people

Risk factor*	Hepatitis B vaccination yes (n=144)	Hepatitis B vaccination no (n=4,629)	p value
Intravenous drug use	20.9%	5.1%	<0.001
Dental therapy	31.9%	33.0%	0.771
Haemodialysis	4.6%	0.2%	<0.001
Household HBsAg+	33.0%	9.5%	<0.001
≥3 sex. partners	31.1%	28.8%	0.633
Condom use (never/occas.)	18.7%	20.8%	0.565
Parenteral exposure	26.9%	32.4%	0.175
Nosocomial expos.	14.3%	17.8%	0.282

* cases may have more than one risk factor

Co-infections among the 144 vaccinated hepatitis B cases

Co-infections	n°	%
Delta	3	2.1%
HCV	25	17.4%
Delta + HCV	2	1.4%
Total	30	20.8%

Hepatitis B cases in vaccinated people: How many doses?

Vaccine B	n°	%
1 dose	27	18.8
2 doses	37	25.7
3 doses	52	36.1
not known	28	19.4
Total	144	100.0

Hepatitis B cases in vaccinated people: Length of time between the doses and the symptoms

Length of time between 1° and 2° dose (months)	
median (range)	**1 (0-26)**
Length of time between 2° and 3° dose (months)	
median (range)	**5.5 (1-41)**
Length of time between the last dose and symptoms (months)	
median (range)	**6.3 (0-269)**

What is a "true" breakthrough infection?

"True" breakthrough infection refers to a case in a properly vaccinated subjects:

- ✓ **check the vaccination schedule**
- ✓ **check the length of time between vaccination and symptoms**

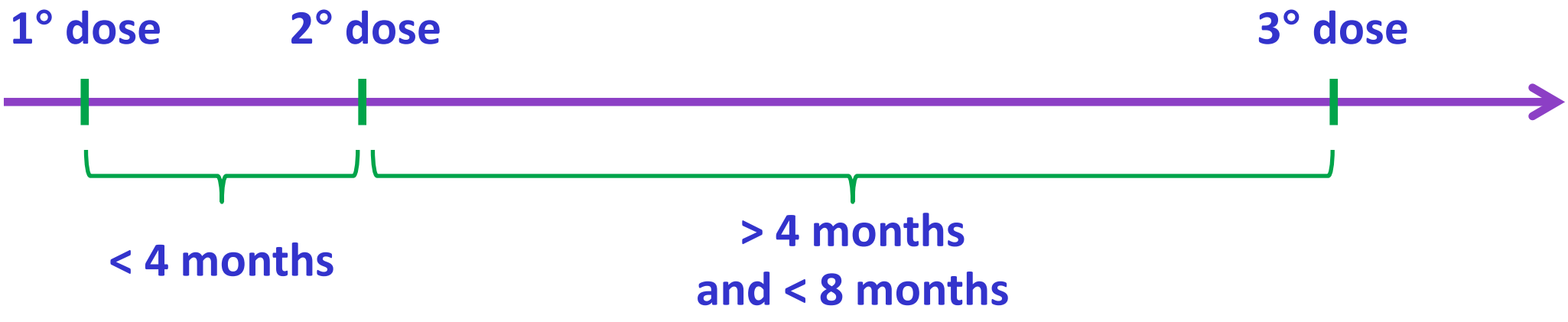
Hepatitis B cases in vaccinated people: Was the schedule correct?

Correct vaccine schedule

3 doses

length of time 1°-2° dose < 4 months

length of time 2°-3°dose > 4 months and < 8 months



Hepatitis B cases in vaccinated people: Was the schedule correct?

administ. doses	correct schedule		
	no	yes (% tot.)	Total
1 dose	27	0	27
2 doses	37	0	37
3 doses	19	29	48
Total	83	29	112

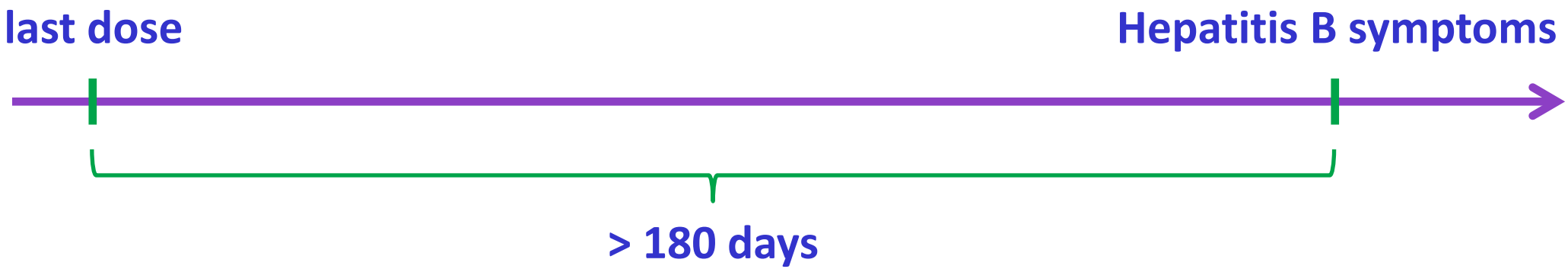
25.9%

Hepatitis B cases in vaccinated people: Was the vaccine administered post exposure?

Post exposure vaccination

Yes: length of time between the last dose and symptoms onset ≤ 180 days

No: length of time between the last dose and symptoms onset > 180 days



Hepatitis B cases in vaccinated people: Was the vaccine administered post exposure?

Administ. doses	Post exposure			
	no	yes	(% yes)	Total
1 dose →	5	17	(77.3)	22
2 doses →	5	31	(86.1)	36
3 doses →	44	4	(8.3)	48
Total	54	52	(49.1)	106

41.5%

Hepatitis B cases in vaccinated people: Vaccination failure

Correct schedule	Post exposure			
	no	yes	not known	Total
no	26	50	7	76
yes	27	2	0	29
not known	1	0	31	32
Total	53	52	38	144

24.1%

Hepatitis B cases in vaccinated people: Vaccination failure

27 cases is the 24.1% of cases with sufficient information

24.1% of the total 144 cases

35 cases

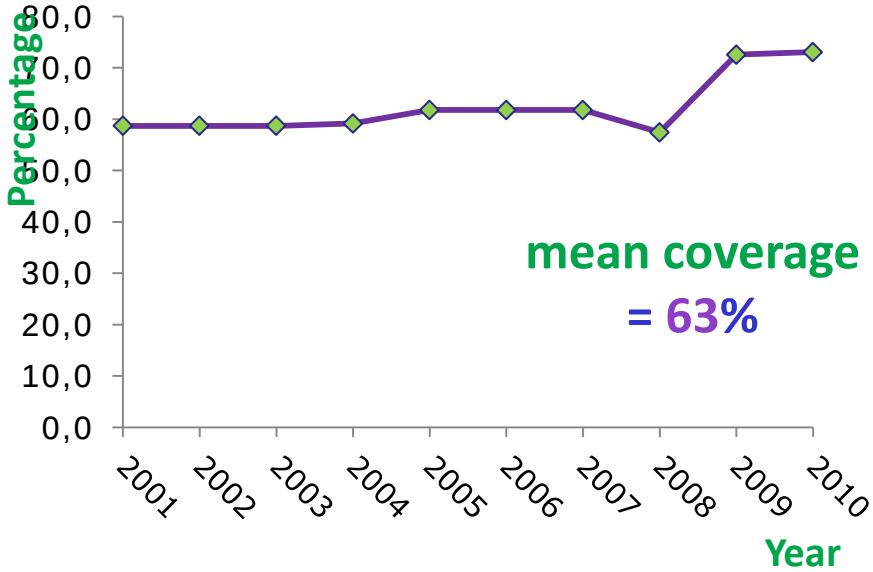
Hepatitis B cases in vaccinated people: How many vaccination failures in Italy?

SEIEVA estimated 35 vaccination failures in ten years

A mean of ~3-4 vaccination failures every year

5-6 vaccination failures in Italy, every year

Percentage of Italian population covered by SEIEVA (yearly trend)



Description of the 27 hepatitis B cases correctly vaccinated

Age (year)	
median (range)	24 (2-79)
Compulsory vaccination	
yes	14 (51.9%)
no	13 (48.1%)

Sex	M	21	77.8%
	F	6	22.2%

Co-infections	N°
Delta	2
HCV	4
Delta + HCV	0

Risk factors reported by the 27 hepatitis B cases correctly vaccinated

Risk factor*	%
Intravenous drug use	15.4%
Dental therapy	34.6%
Haemodialysis	0.0%
Household HBsAg+	26.3%
≥3 sex. partners	15.4%
Condom use (never/occas.)	4.8%
Parenteral exposure	23.1%
Nosocomial exposure	11.5%

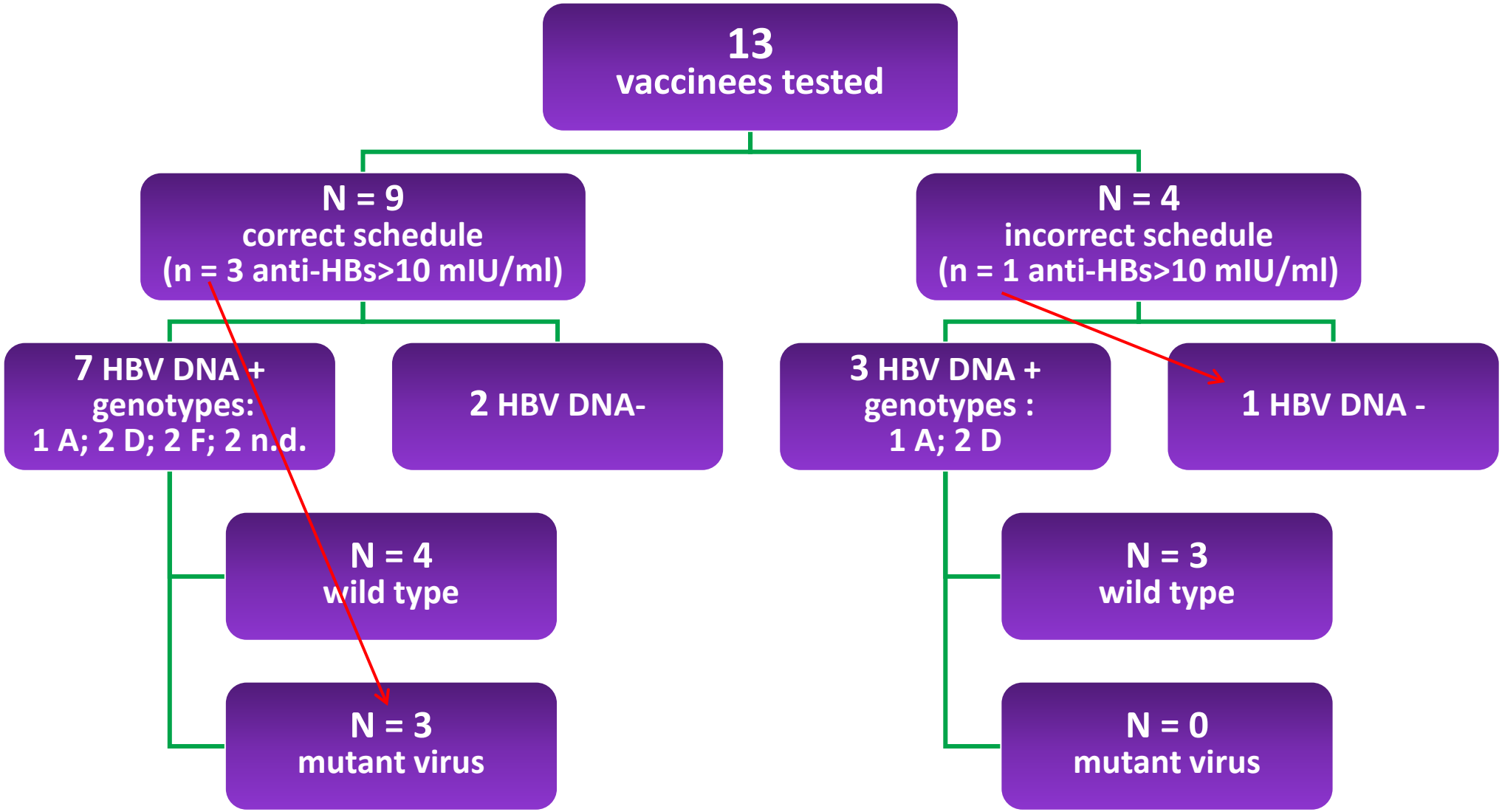
* cases may have more than one risk factor

Molecular characterisation of 13 cases

n	age	gender	vaccine	risk factors	anti-HBs	HBV DNA	genotype	sequence
1	2	F	3 doses	household HBsAg+	>10mIU/ml	pos	nd	G145R
2	36	M	3 doses	IVDU	neg	neg		
3	34	F	2 doses	IVDU	>10mIU/ml	neg		
4	28	M	post-exp	sexual risk, dental care	neg	pos	A	wild type
5	65	M	3 doses	haemodialysis	>10mIU/ml	pos	nd	Thr118Lys
6	16	F	3 doses	household HBsAg+	<10 mIU/ml	neg		
7	24	F	post-exp	IVDU	neg	pos	D	wild type
8	36	M	3 doses	IVDU, sexual risk	neg	pos	D	wild type
9	47	F	post-exp	household HBsAg+	neg	pos	D	wild type
10	2	M	3 doses	household HBsAg+	neg	pos	A	wild type
11	21	M	3 doses	no; blood donor	>10mIU/ml	pos	F	T126A
12	49	M	4 doses	sexual risk, dental care	<10mIU/ml	pos	F	wild type
13	23	M	3 doses	household HBsAg+	neg	pos	D	wild type

age: median (range) = 28 (2-65) **gender = 8 M (62%); 5 F (38%)**

Molecular characterisation of acute hepatitis B cases in vaccinated subjects



Conclusions

- ✓ the study of breakthrough infections has confirmed the vaccine effectiveness
- ✓ the vaccination failures are rare events: in Italy 5-6 cases every year (estimated by SEIEVA data)
- ✓ Out of the 7 subjects correctly vaccinated and HBV DNA positive, almost half of the infections (4) were attributable to a lack of immune response and the other half (3) to viral mutation able to evade the immune response
- ✓ surveillance systems like SEIEVA are very useful in monitoring the vaccine effectiveness