Acellular pertussis vaccine administerd at birth; perspectives

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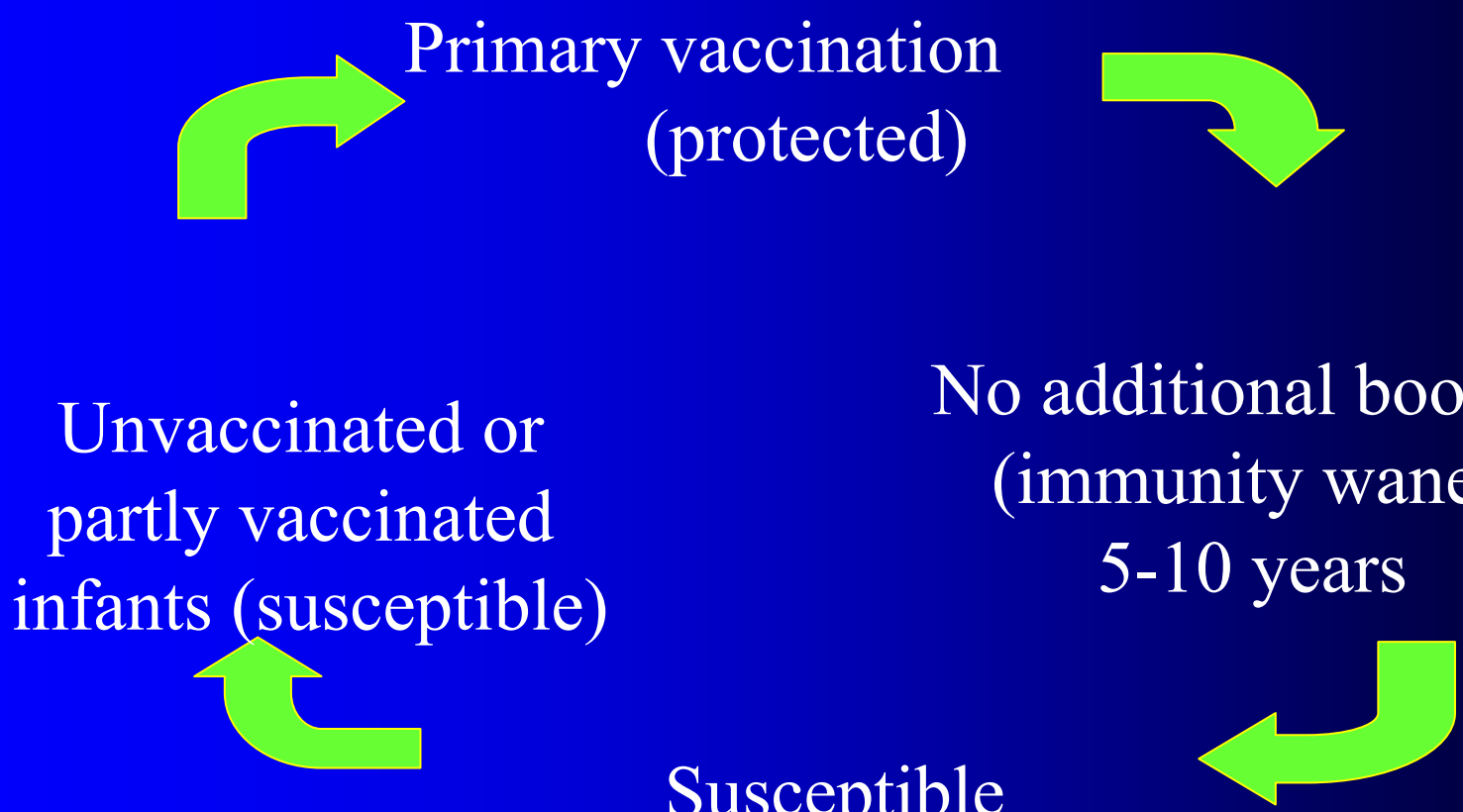
Vaccination against pertussis in children before 24 months

Greatly reduced:

- Pertussis incidence
- Serious illness
- Complications (pneumonia, seizures, encelopathy)
- Infant mortality

Transmission cycle of pertussis between adults and infants



Pertussis cases by age group USA 1997-2000

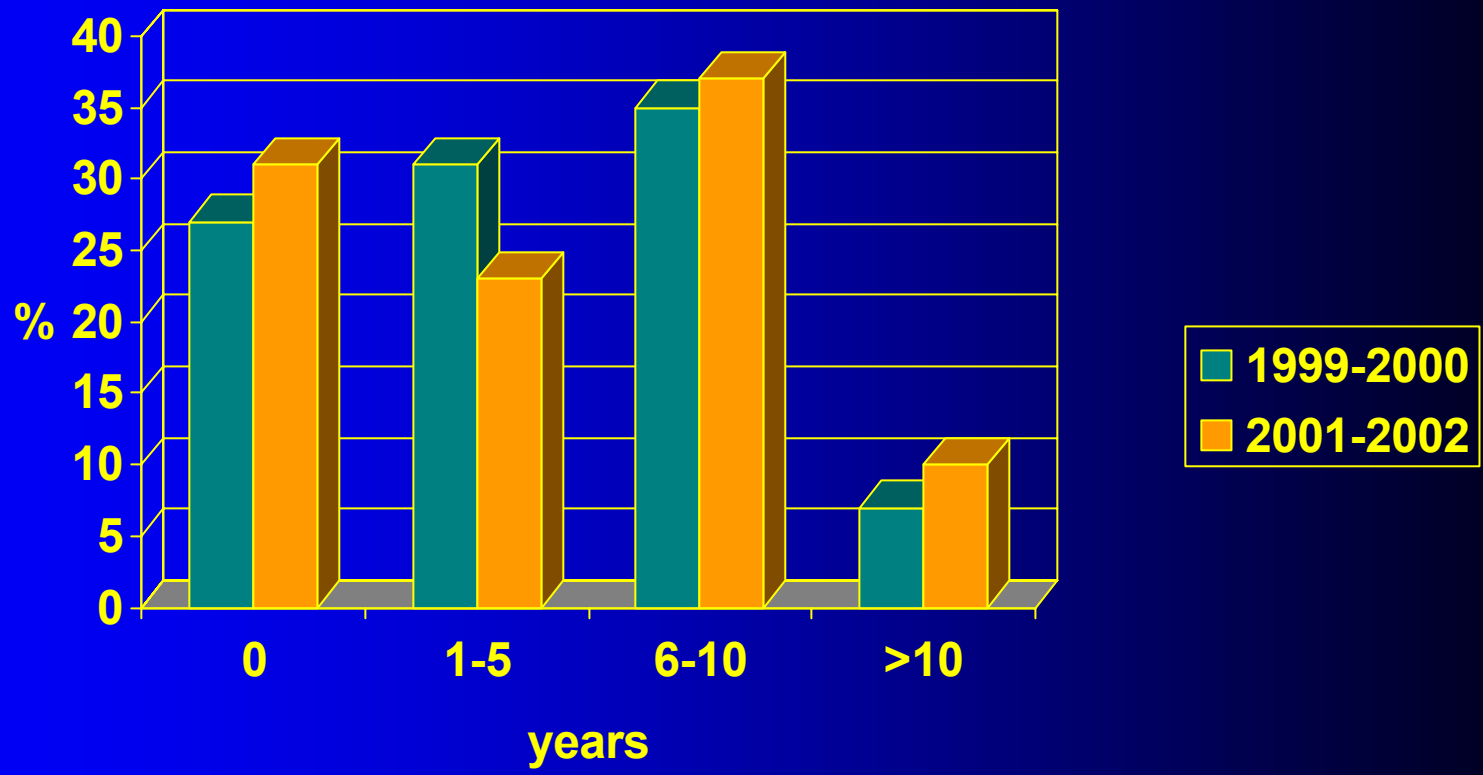
Age	Cases (%)	Hosp.	Pneu.	Seiz.	Deaths
<6 m	*7203 (26)*	*4543 (63)*	*847 (12)*	*103 (1)*	*56 (1)*
6-11m	1073 (4)	301 (28)	92 (9)	7 (0.7)	1 (0.1)
1-4y	3137 (11)	324 (10)	168 (5)	36 (1.2)	1 (<0.1)
5-9y	2756 (10)	86 (3)	68 (3)	13 (0.5)	2 (0.1)
10-19y	*8273 (29)*	*174 (2)*	*155 (2)*	*25 (0.3)*	*0*
>20y	5745 (20)	202 (3)	147 (3)	32 (0.6)	2 (<0.1)
tot	28187	5630	1477	216	62

Edwards KM; Vaccine 2003;21:3483

Pertussis cases: 1992-1995 and 1996-1999 Emilia Romagna (Northern Italy)

- Incidence of pertussis in infants under 6 months was about 1 per 1000 live births in the period 1996-1999.
- In the same area the median age at onset of infection shifted from 4.8 years in 1992-1995 to 7.2 years in 1996-1999

Pertussis cases: 1999-2000 and 2001-2002 Puglia (Southern Italy)



Il giornale della vaccinazione vol 3 n°4; July 2003

Pertussis cases in the first year of life

Puglia region : years 1999-2001

0-6 months of life =88%

7-12 months of life =12%

Considerations on epidemiological scale can only suggest the earliest possible immunization of infants

Beginning of the neonatal pertussis vaccination era?

- Maternal antibodies to acellular pertussis antigens do not inhibit the infants T cell response and the priming
- Immaturity of infants immune system depends on “naive” lymphocytes for a lack of antigen experience
- The priming makes the naive cells into memory cells
- The level of immune response depends on the number of vaccine doses

Aim of the study

To evaluate:

- the immunogenicity of a 3 component acellular pertussis vaccine administered at birth:
  - filamentous hemagglutinin (FHA), 2,5µg
  - pertactine (PRN), 2,5µg
  - pertussis toxin (PT) genetically detoxified 5µg
- maternal antibodies influence

Study population

- 91 newborns (48 M and 43 F) healthy, full-term, enrolled between January and August 1999.
- Mean gestational age was 39.3±1.4 weeks
- Mean birth-weight was 3293±440 grams.

Study design (I)

GROUP 1: 45 newborns immunized at:

4th day of life

3rd month*

5th month*

11th month*

GROUP 2: 46 newborns immunized at:

3rd month*

5th month*

11th month*

* With Acelluvax DTaP together with anti-HBV, IPV, Hib

Study design (II)

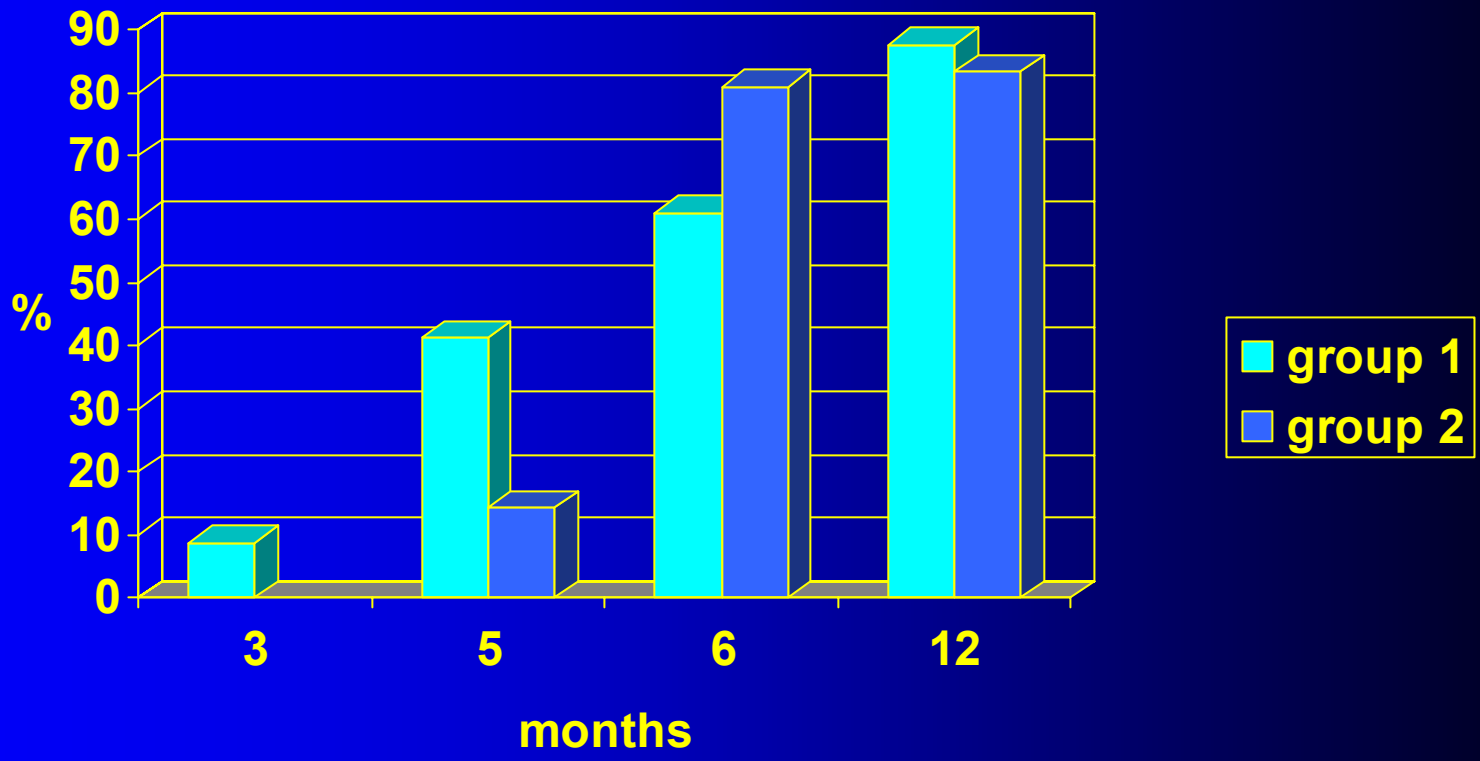
- We drew blood samples from all mothers at delivery and from all infants at birth and at 12 months
- Each infant was randomly assigned to 2 of 3 possible intermediate blood samplings
  - At 3 mo before I dose in group 2 or II dose in group 1
  - A 5 mo before II dose in group 2 or III dose in group 1
  - A 6 mo after II dose in group 2 or III dose in group 1

Serologic testing

- Anti-PRN, anti-FHA, anti-PT IgG levels were detected by ELISA (EU/ml)
- The estimated minimum detection level were:
  - 1,5 EU/ml anti-PT
  - 1 EU/ml anti-FHA
  - 3 EU/ml anti-PRN
- Response was defined as a 4-fold increment in prevaccination antibody level

RESULTS

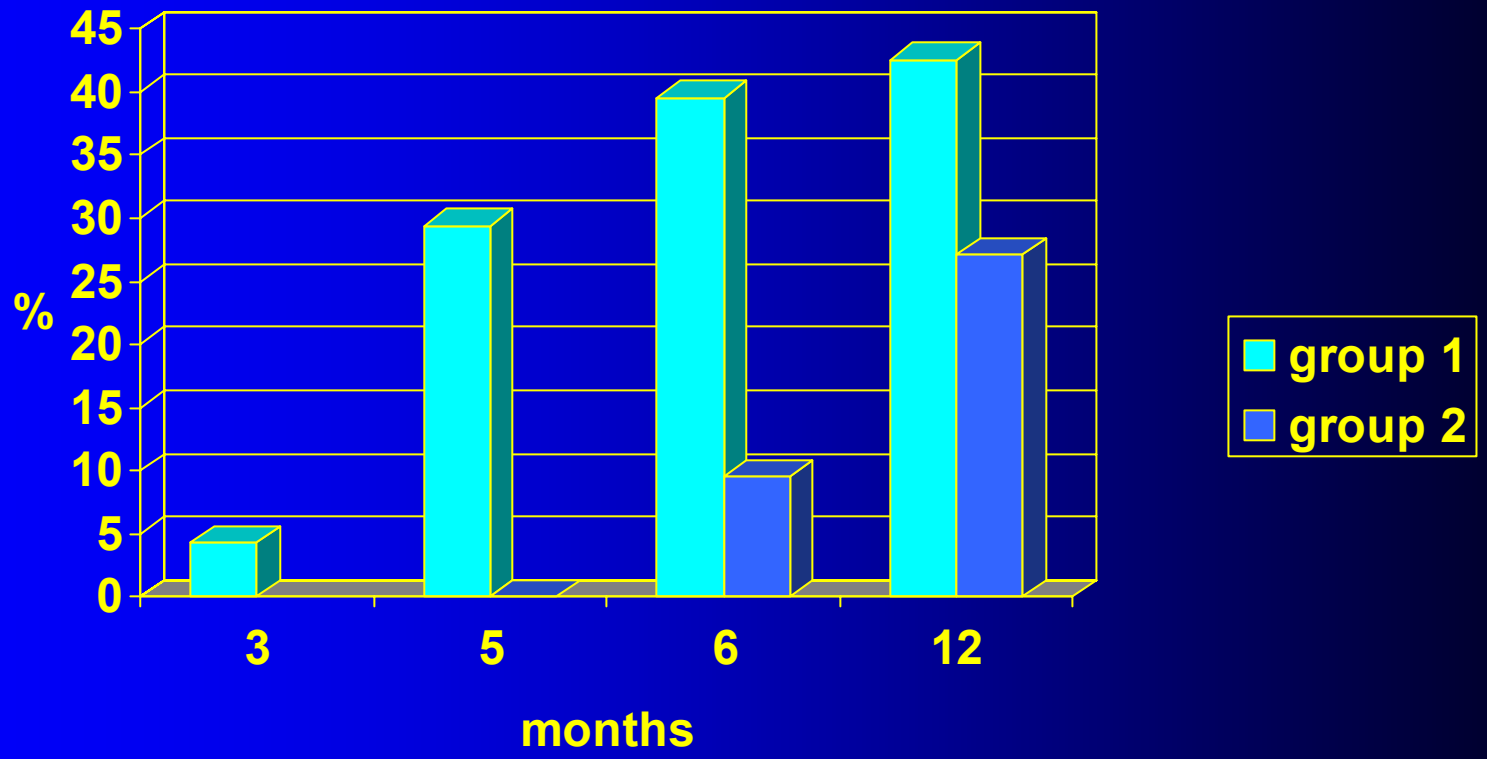
Percentage of infants with 4-fold increment in prevaccination antibody anti-PT level



P=0,0001 test χ^2

RESULTS

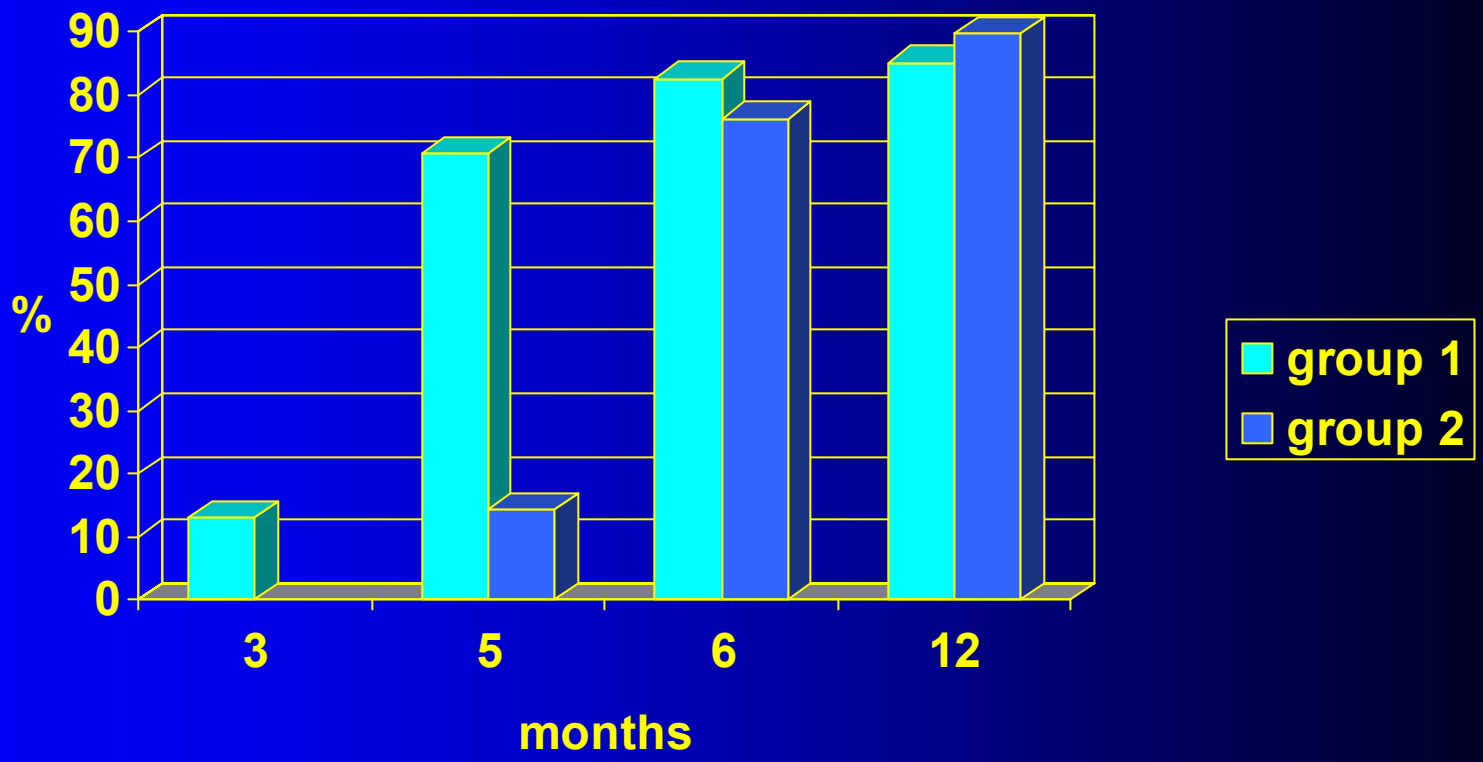
Percentage of infants with 4-fold increment in prevaccination antibody anti-FHA level



P=0.04 test χ^2

RESULTS

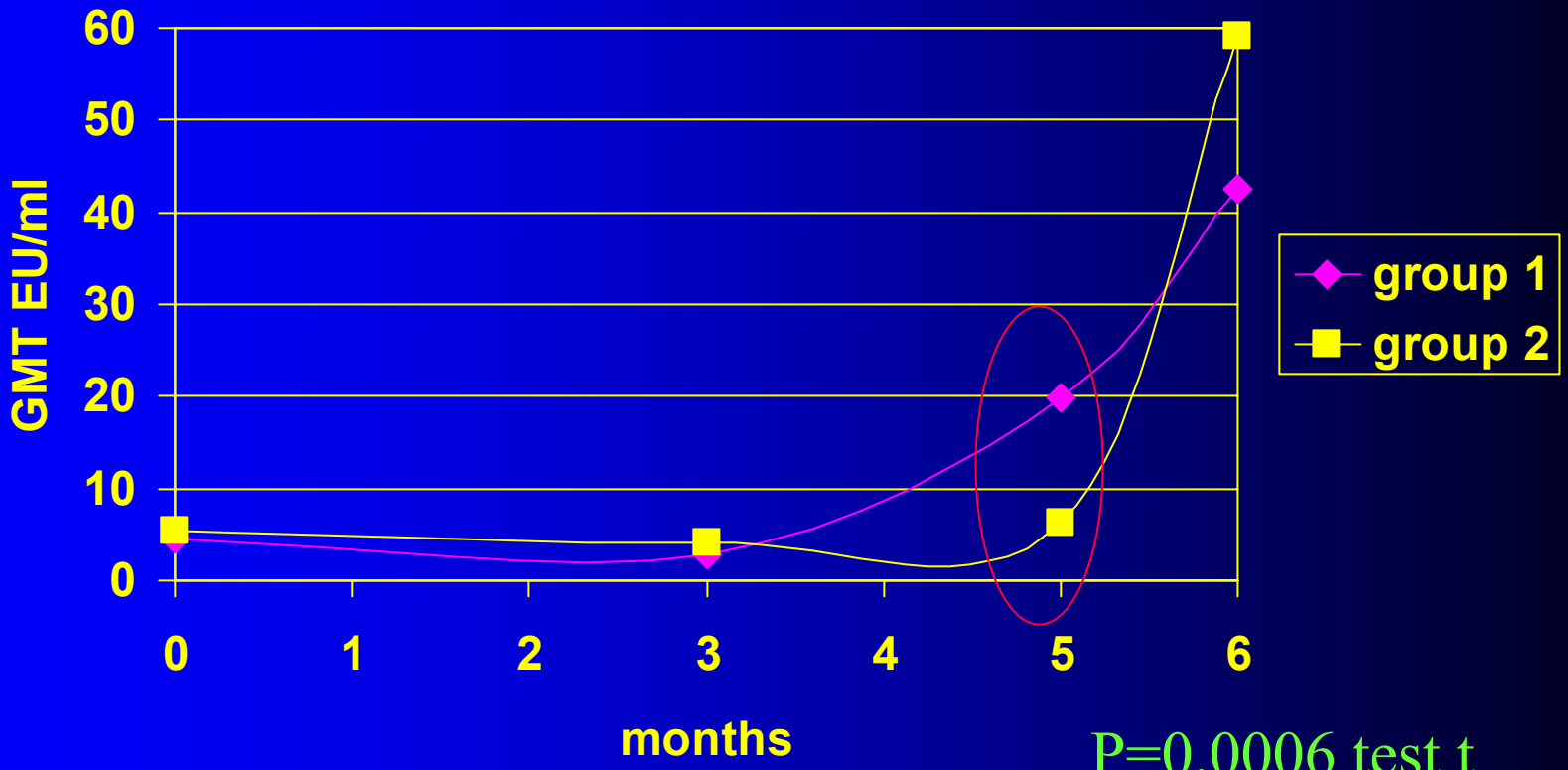
Percentage of infants with 4-fold increment in prevaccination antibody anti-PRN level



P=0.01 test χ^2

RESULTS

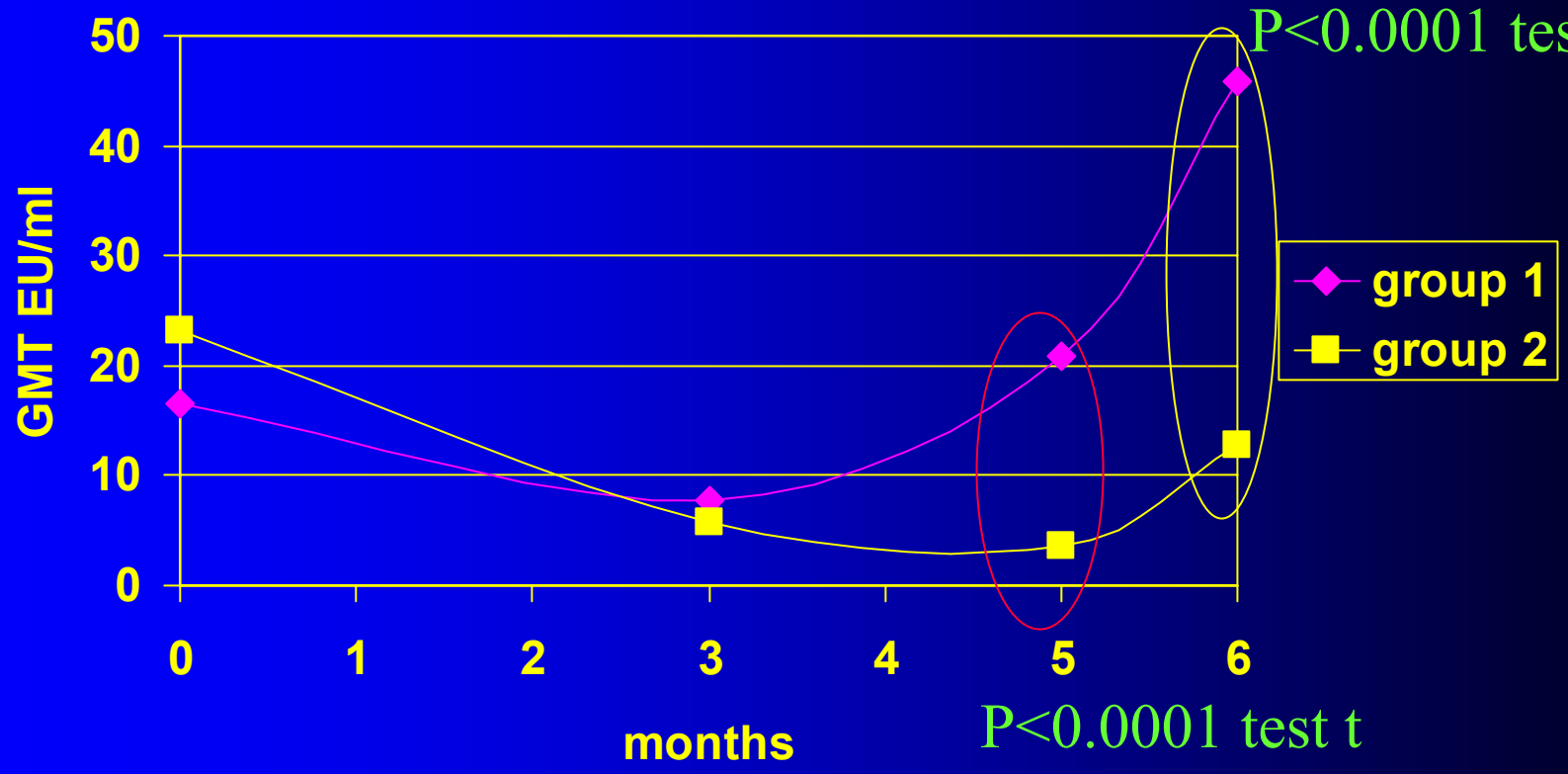
GMT of anti-PT in the 2 groups in the first 6 months of life



P=0.0006 test t

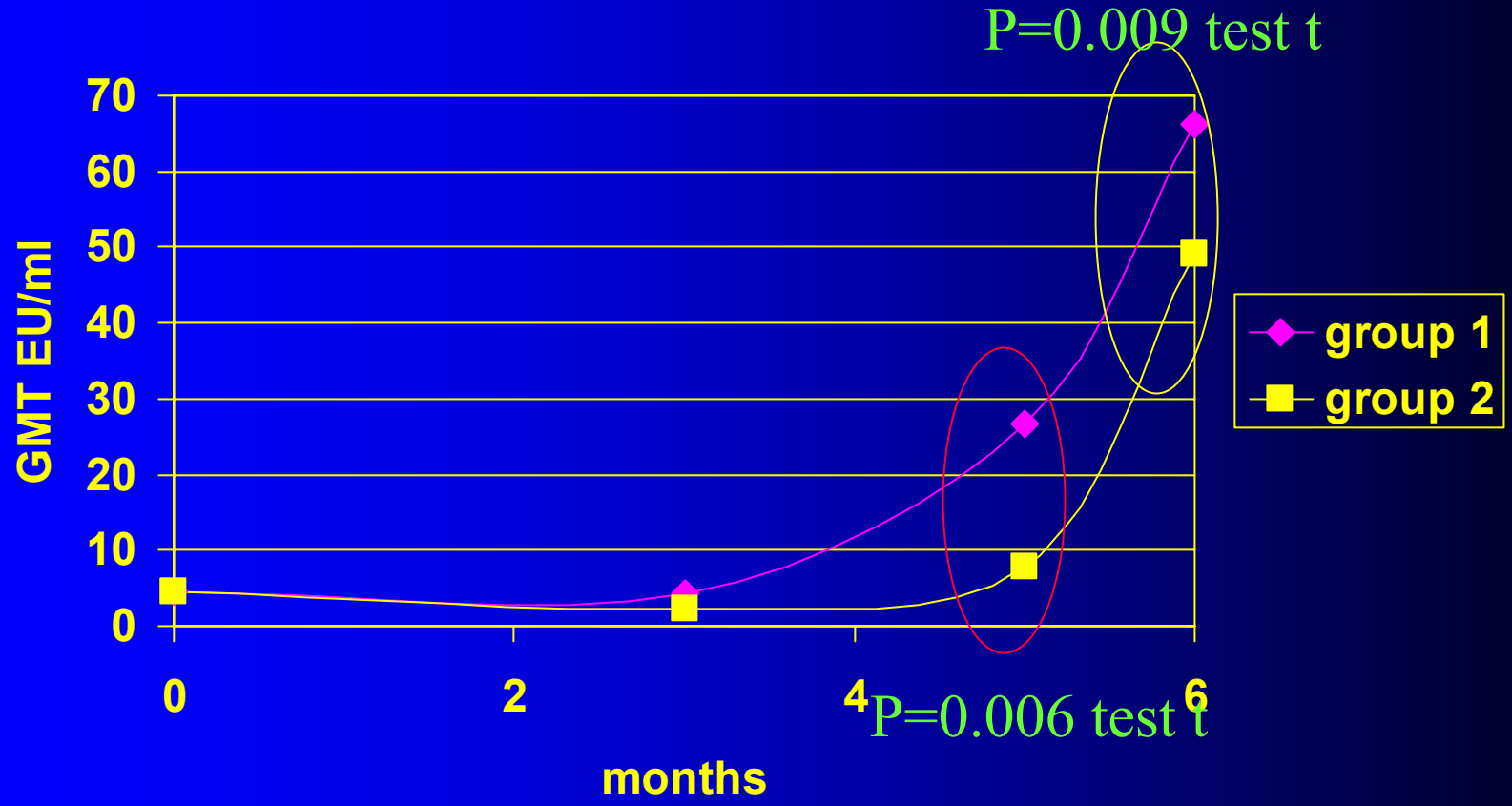
RESULTS

GMT of anti-FHA in the 2 groups in the first 6 months of life



RESULTS

GMT of anti-PRN in the 2 groups in the first 6 months of life



RESULTS

Anti-PT, anti-FHA, anti-PRN levels in the 2 groups at 12 months of age:

- GMT of anti-FHA is higher in group 1 ($p=0,002$)
- GMT of anti-PRN did not show any significant difference
- GMT of anti-PT is significantly lower in group 1 ($p<0,0001$)

RESULTS

GMT of maternal antibodies at delivery

	N	Anti-PT	Anti-FHA	Anti-PRN
Group 1	45	4.5	16.6	4.6
Group 2	46	5.5	23.2	6.4

Conclusions

- Neonatal aP vaccination results in:
  - earlier immune response (than infants vaccinated according routine schedule)
  - efficient immunological priming
- Passively acquired antibodies did not affect neonatal immune response

Strategies for controlling pertussis should consider that:

- Neonatal priming with antipertussis vaccines reduce the window of vulnerability to pertussis at the time of its greatest severity
- We need the boostering of adolescents and adults to achieve long-term protection.