Retour sur la notion de corrélats de protection

O. Epaulard

Infectiologie, CHU de Grenoble

Journée du groupe vaccination-prévention de la SPILF

18 septembre 2026

2010

MINIREVIEW

Correlates of Protection Induced by Vaccination[▽]

Stanley A. Plotkin*

University of Pennsylvania and Vaxconsult, 4650 Wismer Road, Doylestown, Pennsylvania 18902

TABLE 1. Definitions of terms used in this article

Term	Definition
Correlate	An immune response that is responsible for and statistically interrelated with protection
Absolute correlate	A specific level of response highly correlated with protection; a threshold
Relative correlate	A level of response variably correlated with protection
Cocorrelate	One of two or more factors that correlate with protection in alternative, additive, or synergistic ways
Surrogate	An immune response that substitutes for the true immunologic correlate of protection, which may be unknown or not easily measurable

Certaines réponses immunitaires peuvent être associées à la protection sans être responsable de la protection

2012

Nomenclature for Immune Correlates of Protection After Vaccination

Stanley A. Plotkin[1] and Peter B. Gilbert[2,3]

[1]University of Pennsylvania and Vaxconsult, Doylestown; [2]University of Washington, and [3]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle

Table 1. Terminology for Immune Correlates of Protection

Term	Synonyms	Definition
CoP (correlate of protection)	Predictor of protection	An immune marker statistically correlated with vaccine efficacy (equivalently predictive of vaccine efficacy) that may or may not be a mechanistic causal agent of protection[a]
mCoP (mechanistic correlate of protection)	Causal agent of protection; protective immune function	A CoP that is mechanistically and causally responsible for protection
nCoP (nonmechanistic correlate of protection)	Correlate of protection not causal; predictor of protection not causal	A CoP that is not a mechanistic causal agent of protection

[a] A correlate of protection can be used to accurately predict the level of vaccine efficacy conferred to vaccine recipients (individuals or subgroups defined by the immune marker level).

S. Plotkin propose le terme « *nonmechanistic CoP* » pour ces réponses associées à la protection sans en être le support

TABLE 2. Quantitative correlates and surrogates of protection after vaccination

Vaccine	Test	Level required	Reference(s)[a]
Anthrax	Toxin neutralization	1,000 IU/ml	87, 136, 149, 170, 191
Diphtheria	Toxin neutralization	0.01–0.1 IU/ml	14, 92
Hepatitis A	ELISA	10 mIU/ml	45, 110
Hepatitis B	ELISA	10 mIU/ml	66
Hib polysaccharides	ELISA	1 μg/ml	74
Hib conjugate	ELISA	0.15 μg/ml	73
Human papillomavirus	ELISA	ND[b]	140
Influenza	HAI	1/40 dilution	50, 171
Japanese encephalitis	Neutralization	1/10 dilution	63
Lyme disease	ELISA	1,100 EIA U/ml	128
Measles	Microneutralization	120 mIU/ml	24, 120, 158
Meningococcal	Bactericidal	1/4 (human complement)	96
Mumps	Neutralization?	ND	189
Pertussis	ELISA (toxin)	5 units	25, 173, 180.
Pneumococcus	ELISA; opsonophagocytosis	0.20–0.35 μg/ml (for children); 1/8 dilution	68, 81, 167
Polio	Neutralization	1/4–1/8 dilution	41, 95, 139
Rabies	Neutralization	0.5 IU/ml	196,
Rotavirus	Serum IgA	ND	49, 67, 104, 199, 200
Rubella	Immunoprecipitation	10–15 mIU/ml	2, 27, 53, 99, 141, 169
Tetanus	Toxin neutralization	0.1 IU/ml	13, 37,
Smallpox	Neutralization	1/20	89, 93, 139, 160
Tick-borne encephalitis	ELISA	125 IU/ml	77
Tuberculosis	Interferon	ND	46
Varicella	FAMA gp ELISA	≥1/64 dilution; ≥5 IU/ml	195
Yellow fever	Neutralization	1/5	79, 97
Zoster	$CD4^+$ cell; lymphoproliferation	ND	190

Pourquoi a-t-on besoin de corrélats de protection ?

- Réponse la plus évidente : pour prendre des décisions sans étude d'efficacité

- Pour évaluer l'intérêt des vaccins en développement
  - La vaccination permet-elle d'obtenir la réponse protectrice ?

    Et les comparer à des vaccins pré-existants

- Pour optimiser les schémas vaccinaux

- Pour mettre au point de nouveaux vaccins
  - *Reverse immunology*

Comment établir un corrélat de protection ?

- Étude des sujets protégés ou non (hors vaccination) dans une population
  - Nécessite de phénotyper tous les participants pour voir la difference entre infectés ou non : lourd
  - Difficile de voir s'il s'agit d'un *correlate* ou d'un *surrogate* …
- Étude de la protection apportée par la vaccination
  - Idem
- Données issues de l'immunisation passive : HBV…
  - "Graal" : anticorps monoclonal
- Étude de personnes immunodéprimées
  - Ex : quelle protection chez l'agammaglobulinémique ?
- *Animal* (voire *human*…) *challenge studies*
  - L'injection de tel ou tel effecteur est-il protecteur ?

Un exemple aisé : hépatite B et anticorps anti-HBs

- Crédibilité : l'Ag HBs interagit avec les hépatocytes
- Argument d'immunité passive : prophylaxie par les solutions riches en Ac anti-HBs
- Argument d'immunité active : la vaccination anti-HBs protège contre l'infection
- (Et pour ce virus : la sérologie HBs est un marqueur d'infection)

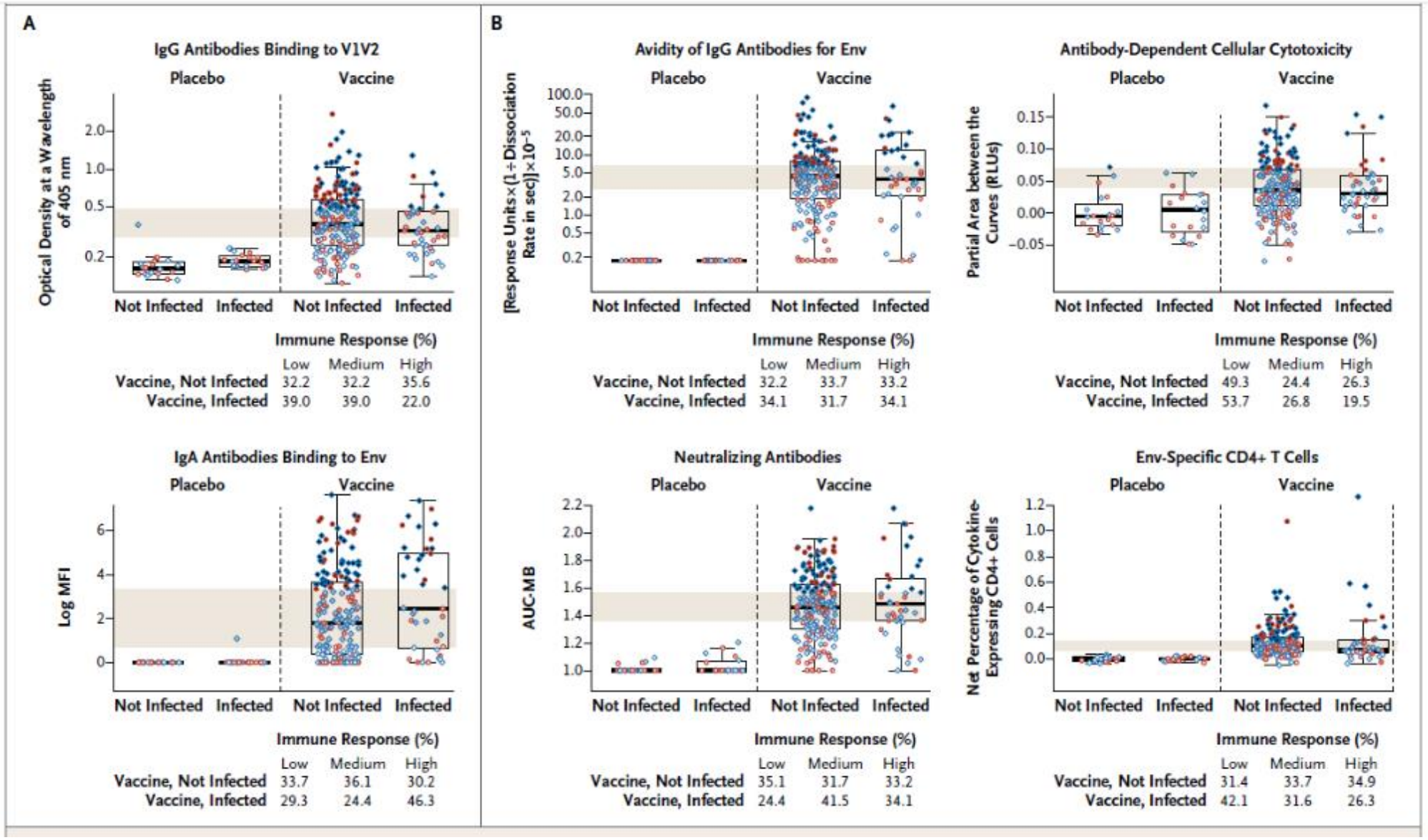
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 5, 2012 VOL. 366 NO. 14

Immune-Correlates Analysis of an HIV-1 Vaccine Efficacy Trial

Barton F. Haynes, M.D., Peter B. Gilbert, Ph.D., M. Juliana McElrath, M.D., Ph.D., Susan Zolla-Pazner, Ph.D., Georgia D. Tomaras, Ph.D., S. Munir Alam, Ph.D., David T. Evans, Ph.D., David C. Montefiori, Ph.D., Chitraporn Karnasuta, Ph.D., Ruengpueng Sutthent, M.D., Ph.D., Hua-Xin Liao, M.D., Ph.D., Anthony L. DeVico, Ph.D., George K. Lewis, Ph.D., Constance Williams, B.S., Abraham Pinter, Ph.D., Youyi Fong, Ph.D., Holly Janes, Ph.D., Allan DeCamp, M.S., Yunda Huang, Ph.D., Mangala Rao, Ph.D., Erik Billings, Ph.D., Nicos Karasavvas, Ph.D., Merlin L. Robb, M.D., Viseth Ngauy, M.D., Mark S. de Souza, Ph.D., Robert Paris, M.D., Guido Ferrari, M.D., Robert T. Bailer, Ph.D., Kelly A. Soderberg, Ph.D., Charla Andrews, Sc.M., Phillip W. Berman, Ph.D., Nicole Frahm, Ph.D., Stephen C. De Rosa, M.D., Michael D. Alpert, Ph.D., Nicole L. Yates, Ph.D., Xiaoying Shen, Ph.D., Richard A. Koup, M.D., Punnee Pitisuttithum, M.D., D.T.M.H., Jaranit Kaewkungwal, Ph.D., Sorachai Nitayaphan, M.D., Ph.D., Supachai Rerks-Ngarm, M.D., Nelson L. Michael, M.D., Ph.D., and Jerome H. Kim, M.D.

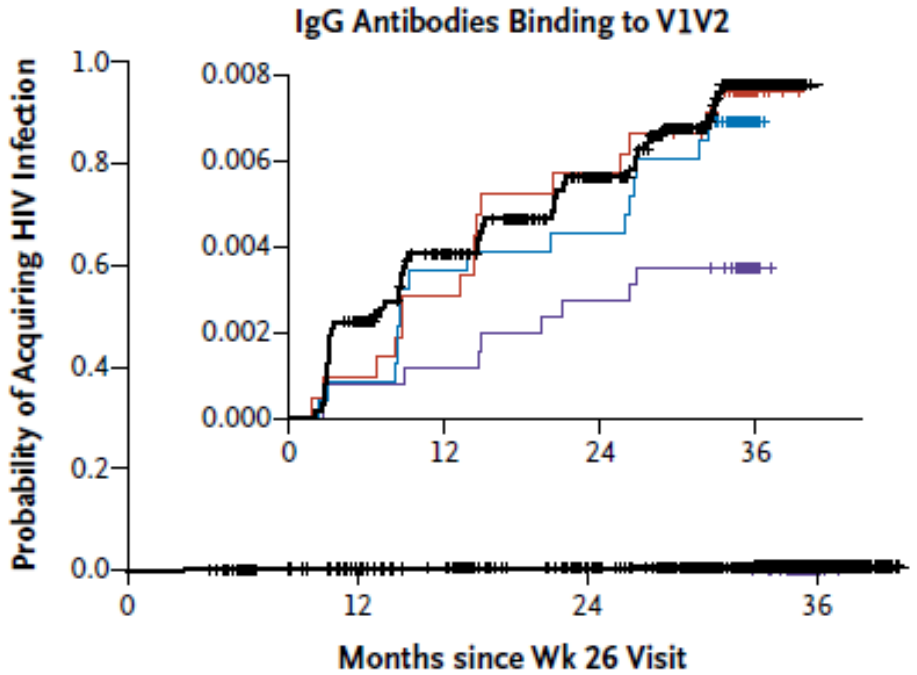
Devant le potentiel (et partiel) succès de l'essai RF144, des corrélats de protection ont tenté d'être établis…



En particulier, une réponse dirigée contre les régions V1V2 de la gp120 a été identifiée comme un potentiel corrélat de protection …

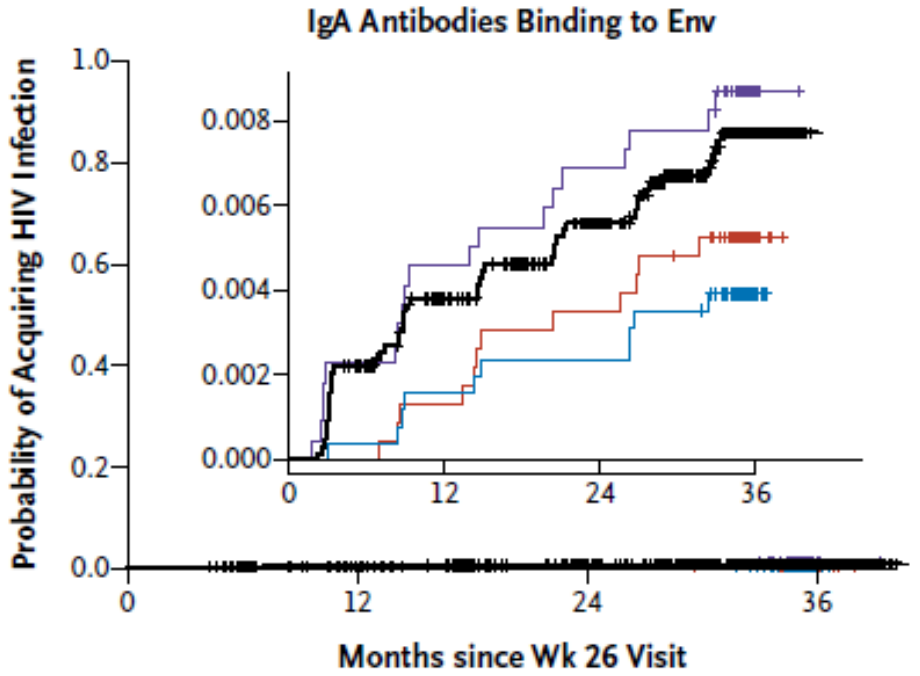
Placebo
Vaccine, medium response
Vaccine, low response
Vaccine, high response

A



No. at Risk (no. of infections)

Placebo	6267 (0)	6199 (24)	6127 (11)	693 (13)
Low response	2111 (0)	2105 (6)	2099 (6)	210 (4)
Medium response	2312 (0)	2304 (8)	2302 (2)	180 (6)
High response	2563 (0)	2560 (3)	2556 (4)	264 (2)



No. at Risk (no. of infections)

Placebo	6267 (0)	6199 (24)	6127 (11)	693 (13)
Low response	2276 (0)	2273 (3)	2268 (5)	282 (4)
Medium response	2539 (0)	2535 (4)	2533 (2)	202 (4)
High response	2172 (0)	2162 (10)	2157 (5)	170 (4)

Review

V2-Specific Antibodies in HIV-1 Vaccine Research and Natural Infection: Controllers or Surrogate Markers

Ralf Duerr * and Miroslaw K. Gorny

Mais par la suite, de nombreux vaccins élaborés pour générer une telle réponse ne se sont pas révélés protecteurs chez l'animal

Table 3. Non-human primate vaccine studies with SHIV or SIV challenges.

#	Author	Immunization	Challenge	% Protection	Immune Correlates	V2 Antigens Tested	V2 Abs Correlation
				HIV Env			
1	Barouch DH Cell, 2013	Ad/MVA (mosaic)	$SHIV_{SF162P3}$	3 chall. 45% 6 chall. 18%	Env Abs Neutral SF162, ADCP	V2 peptides V1V2-gp70	NO
2	Bradley T Nat Comm, 2017	ALVAC/Pentavalent (B and AE clade)	$SHIV_{1157}$ (clade C)	55%	Cell-bound Env Abs, ADCC MIP-1b in NK cells	V2 peptides	NO
3	Barouch DH Lancet 2018	Ad26, gp140 mosaic	$SHIV_{SF162P3}$	67%	Env Abs T-cell response	V1V2-gp70	NO
4	Malherbe DC J. Virol., 2018	Replicating SAd7 Non-replicating Ad4 (1086, clade C)	$SHIV_{157ipEL}$	Sad—40% Ad4—30%	V2 Abs (SAd7)	V1V2 recombinant (1086.C, JRFL, AE244, 14/00/4)	YES—SAd7 NO—Ad4
5	Hessell A/Gorny MK (Keystone abstract 2019)	DNA gp160, AE gp120, clade AE, B	$SHIV_{BaL.P4}$	55%	SHIV capture Abs Neutral. HIV-SF162	V1V2 scaffolds V2 peptides (CaseA2, AE244, 1086, ZM109)	NO
6	Hessell A/Gorny MK (Keystone abstract 2019)	DNA V1V2, AE V1V2 scaffolds, AE, B	$SHIV_{BaL.P4}$	45%	Not determined yet	V1V2 scaffolds V2 peptides (CaseA2, AE244, 1086, ZM109)	NO
				SIV Env			
7	Barouch DH Nature, 2012	Ad/poxvirus SIVsmE543	SIVmac251 grown in human cells	80%	Env Abs	V2 peptide	YES
8	Roederer M Nature 2014	DNA/Ad5 SIVmac239	SIVmac660	Vaccine efficacy: 69% (mac239)	Env Abs (C3, CD4bs) Neutralization	V1V2mac239	YES
9	Singh S. J. Virol. 2018	DNA, gp120 SIVmac251	SIVsmE660	0%	Neutral. SIVsm660 T cells response	V1V2-gp70 SIVmac251, smE660	YES Mucosal V2 Abs
10	Pegu P. J. Virol. 2013	ALVAC, gp120 SIVmac251	SIVmac251	27% (3 of 11)	Env Abs avidity	V2 peptides SIVmac251	YES
11	Gordon SN. J. Immunol. 2014	HPV, ALVAC, gp120 SIVmac251	SIVmac251	25%	Env-T cells	V1V2 mini protein SIVmac239	YES
12	Gordon SN J. Immunol. 2016	ALVAC, gp120 SIVmac251	SIVmac251	44%	Only V2 Abs	V1V2-gp70 V2 peptides SIVmac251, smE543	YES mucosal V2 Abs-Yes serum V2 Abs-No
13	Kwa S J. Virol. 2015	CD40L DNA MVA SIVmac239	SIVmac251	50%	V2p Abs, gp41 Abs, V1 Abs, gut CD8 T cells	V2 peptides	YES Serum V2p Abs
14	Vaccari M. Nat Med, 2016	ALVAC, gp120 SIVmac251 (alum, MF59)	SIVmac251	44% (alum) 0% (MF59)	Mucosal NKp44+IL17 (alum)	V1V2-gp70 V2 peptides SIVmac239, 251, smE660	YES (Alum, mucosal V2) NO (MF59, mucosal V2 increased risk)
15	Vaccari M Nat Med, 2018	ALVAC, DNA, Ad26 +gp120 SIVmac251, smE660	SIVmac251	52% DNA and ALVAC	Activation CD14 monocytes	V2 peptides SIVmac251, smE543	YES

Defining Surrogate Serologic Tests with Respect to Predicting Protective Vaccine Efficacy: Pertussis Vaccination

1995

PATRICK OLIN
Department of Epidemiology
Swedish Institute for Infectious Disease Control
S-105 21 Stockholm, Sweden

De la difficulté d'identifier des CdP dans la coqueluche : les anticorps anti-TP ou anti-FHA ont le même taux chez des personnes ultérieurement infectées ou non …

TABLE 1. Postvaccination Antibody Levels 60–120 Days after the Second Dose of Acellular Vaccines in Subsequently Culture-Confirmed Cases and a 10% Random Sample of Noncases in Swedish Pertussis Trial 1986–1987[a]

	JNIH-6		JNIH-7		Placebo Noncases and Cases
	Noncases	Cases	Noncases	Cases	
No. of children	122	17	143	25	120
Antitoxin NT (GMT)	81	118	164	211	1
ELISA PT IgG (GMT)	77	81	185	276	5
ELISA FHA IgG (GMT)	25	20	2	2	2

[a] After Reference 1.

ABBREVIATIONS: JNIH-6: a two-component vaccine from Japan National Institute of Health (JNIH), containing inactivated pertussis toxin (iPT) and filamentous haemagglutinin (FHA). JNIH-7: a monocomponent iPT vaccine from JNIH. Antitoxin NT: neutralizing antibody titers in the Chinese Hamster Ovary Cell test. ELISA: enzyme-linked immunosorbent assay. GMT: geometric mean titer.

Corrélat de protection : pour protéger contre quoi ?

- La colonisation / le portage ?
- L'infection ?
- La maladie (= infection symptomatique) ?
- La maladie grave ?

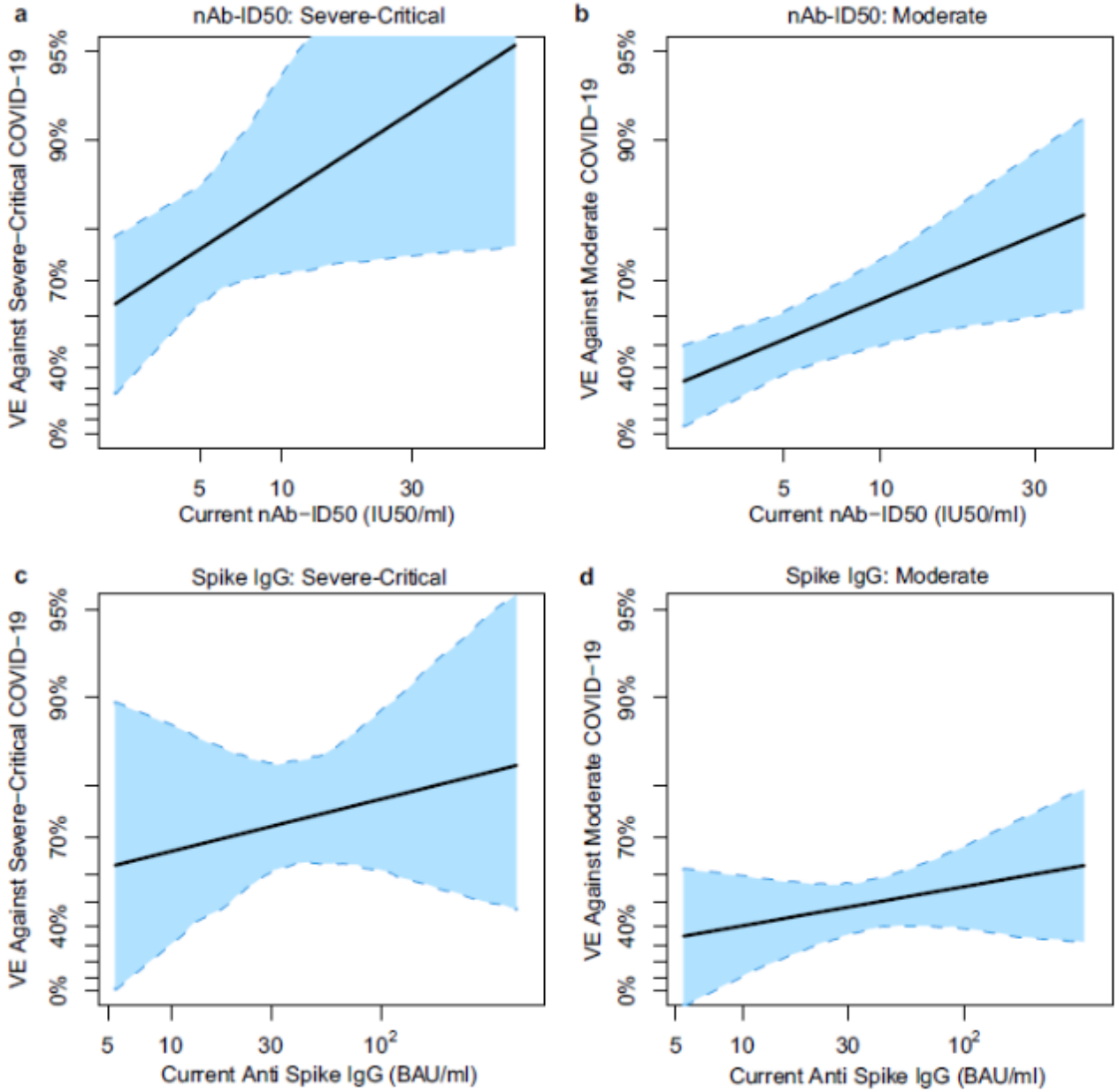
nature communications

Article

https://doi.org/10.1038/s41467-024-53727-y

Neutralizing antibody correlate of protection against severe-critical COVID-19 in the ENSEMBLE single-dose Ad26.COV2.S vaccine efficacy trial

L'efficacité vaccinale varie selon le taux d'anticorps, mais la pente de corrélation est plus importante quant à la protection contre les formes graves que contre les formes modérées



Différentes problématiques

- Toxines bactériennes
- Bactéries encapsulées
- Virus

Toxines bactériennes

Roux et Yersin identifient les toxines diphtérique e tétanique …

3me ANNÉE. JUIN 1889. N° 6

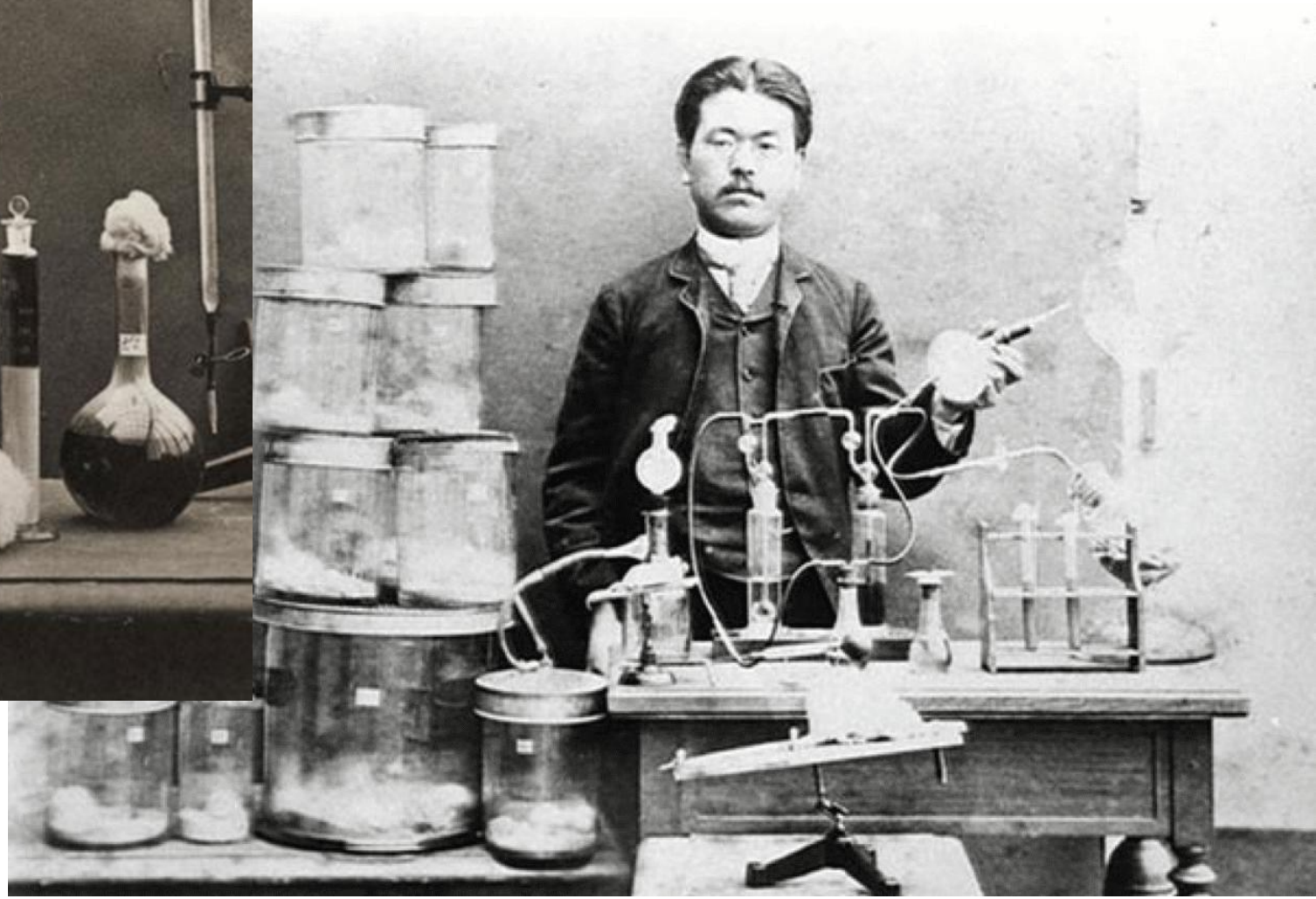
ANNALES
DE
L'INSTITUT PASTEUR

CONTRIBUTION A L'ÉTUDE DE LA DIPHTÉRIE

(2e MÉMOIRE),

PAR E. ROUX ET A. YERSIN.

Puis Kitasato et Behring mettent en evidence l’apparition d’”antitoxines” chez les animaux exposés aux formes dégradées de ces toxines : on commence alors à établir un corrélat entre taux d’antitoxine et protection



Sonderabdruck aus der
„Deutschen Medicinischen Wochenschrift“ 1890, No. 49.
Redacteur: Sanitätsrath Dr. S. Guttmann.

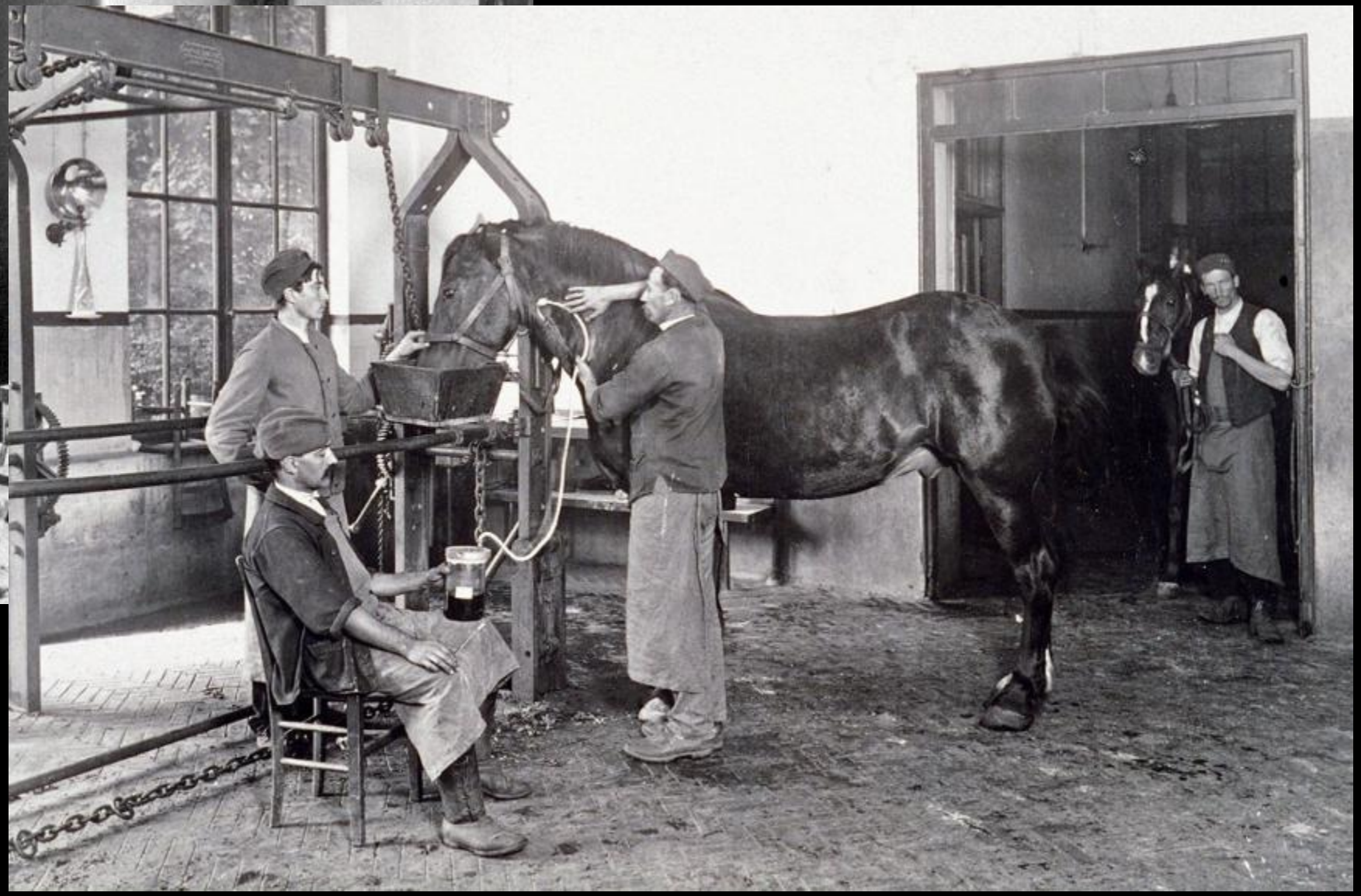
Aus dem hygienischen Institut des Herrn Geheimrath Koch in Berlin.

Ueber das Zustandekommen der Diphtherie-Immunität und der Tetanus-Immunität bei Thieren.

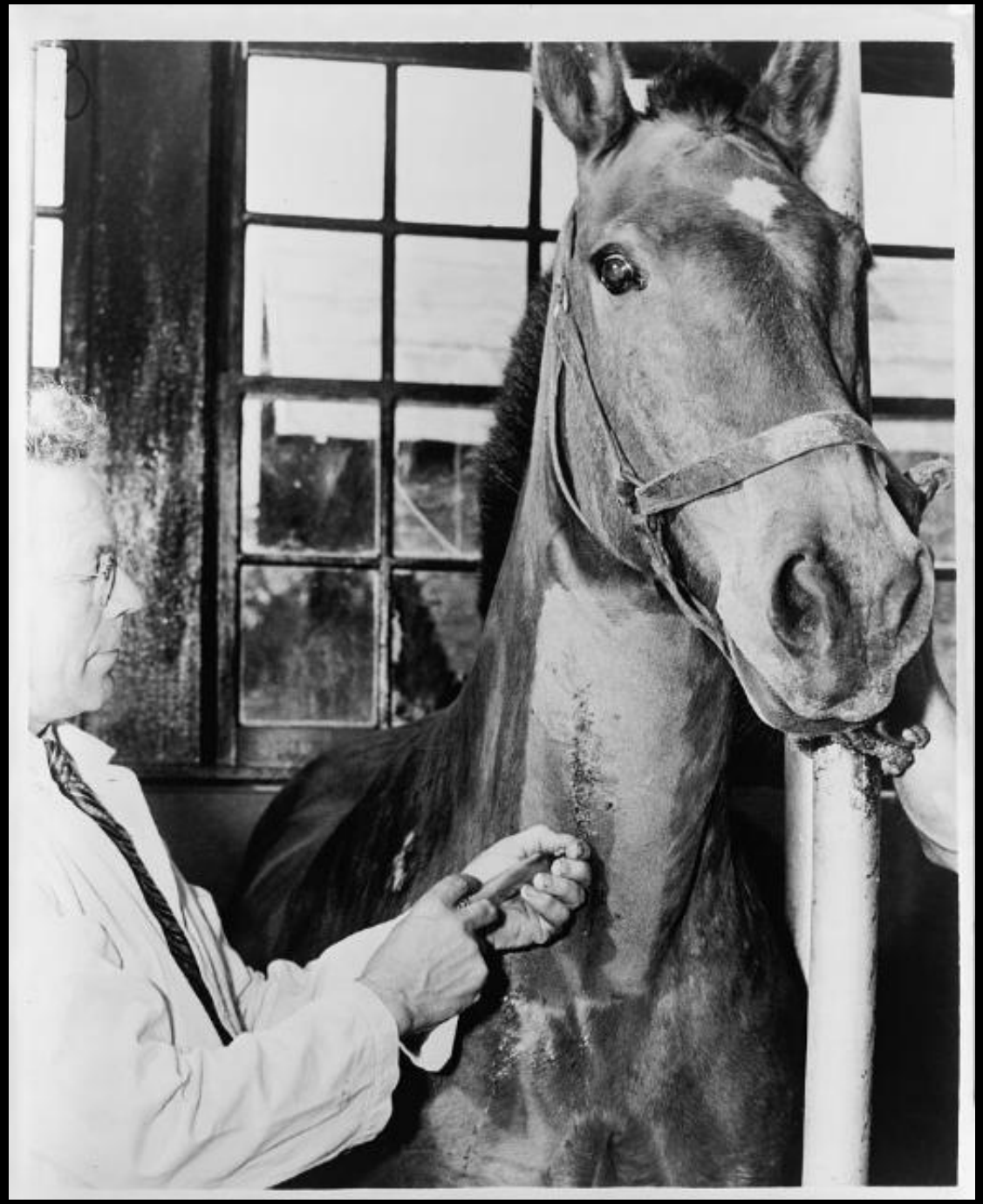
Von

Stabsarzt Dr. **Behring**, Assistenten am Institut,
und Dr. **Kitasato** aus Tokio.

Le succès de la sérothérapie par sérum de cheval sera tel que Behring sera même représenté en boutiquier d'anticorps …



Et Gaston Ramon et d’autres perfectionneront cette tetchnique



THE LANCET]

ORIGINAL

Glenny identifiera l'intérêt de l'aluminium en adjuvantation

PREPARATION OF ALUM-PRECIPITATED TOXOID FOR USE AS AN IMMUNISING AGENT

M. BARR,
M.SC. LOND., A.I.C.

C. G. POPE,
D.SC. BRIST.

A. T. GLENNY,
B.SC. LOND.

F. V. LINGGOOD,
B.SC., PH.D. LOND., A.R.C.S.

(Wellcome Physiological Research Laboratories)

Nouv Presse Med. 1972 Dec 16;1(45):3049-50.

[Antitetanus antibodies. Assay before anatoxinotherapy in 64 tetanus patients]

[Article in French]

M Goulon, O Girard, S Grosbuis, J P Desormeau, M F Capponi

PMID: 4675227

Taux d'antitoxine	Patients avec un tétanos
< 0,01 UI/mL	54/64 (84,4 %)
0,01–0,1 UI/mL	9/64 (14,1 %)
0,1–1 UI/mL	1/64 (1,6 %)

Lors d'épidémies, l'exploration du taux d'anticorps chez les malades montrent l'absence d'anticorps anti-toxine, ce qui est un autre argument pour les établir comme support de la protection

The Journal of Immunology

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Volume 54, Issue 4
December 1946

JOURNAL ARTICLE

Circulating Antitoxin at the Onset of Diphtheria in 425 Patients

Get access ›

Johs Ipsen

The Journal of Immunology, Volume 54, Issue 4, December 1946, Pages 325–347,
https://doi.org/10.4049/jimmunol.54.4.325

Published: 01 December 1946 **Article history** ▾

Les mêmes travaux ont été faits pour la diphtérie

Bactéries encapsulées

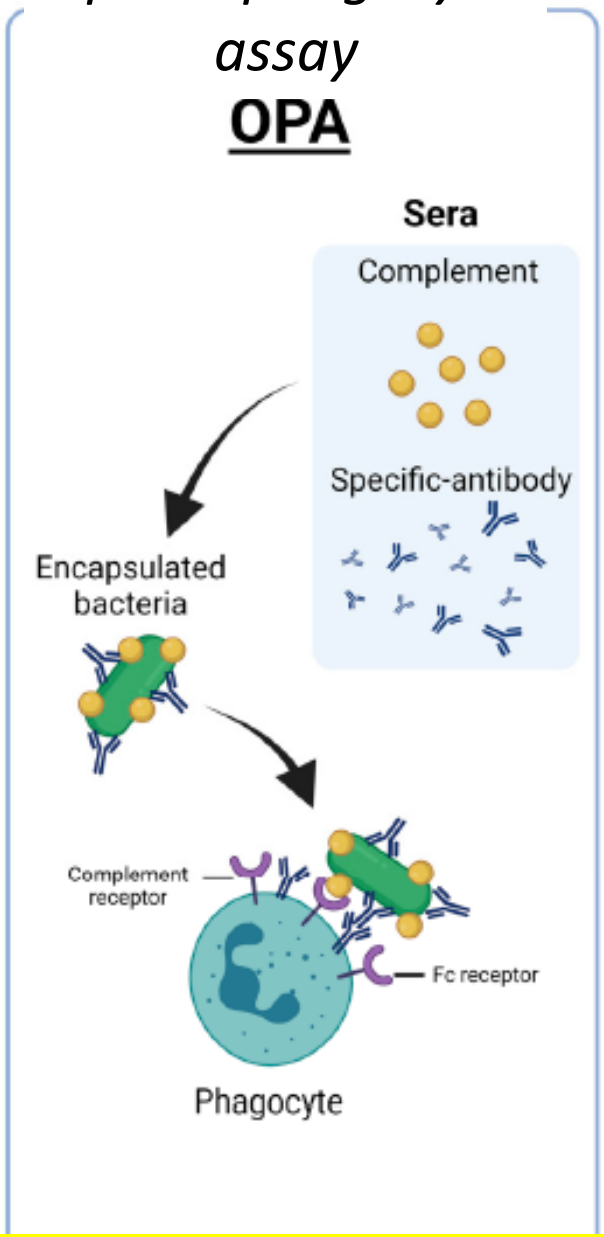
vaccines

Perspective

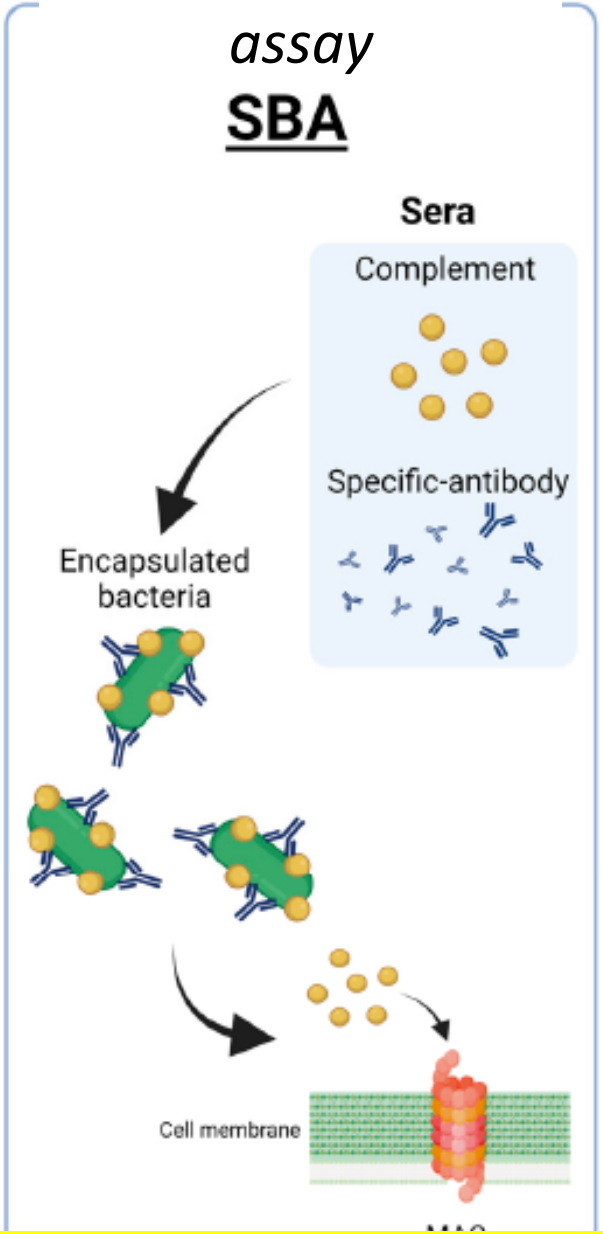
Evaluating Functional Immunity Following Encapsulated Bacterial Infection and Vaccination

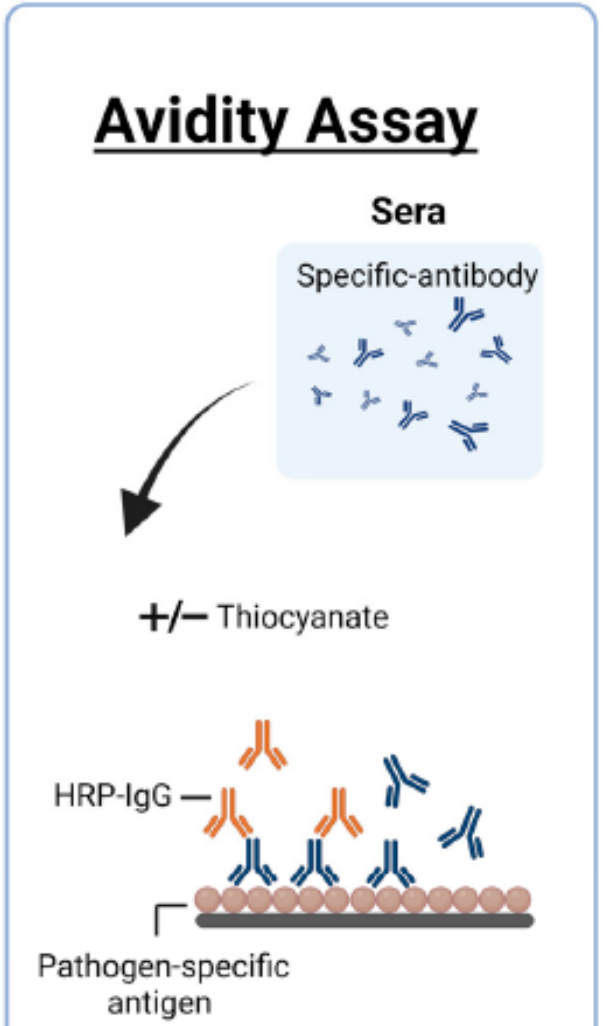
Zheng Quan Toh [1,2,†], Rachel A. Higgins [1,†], Nadia Mazarakis [1], Elysia Abbott [1], Jordan Nathanielsz [1], Anne Balloch [1], Kim Mulholland [1,2,3] and Paul V. Licciardi [1,2,*]

Opsonophagocytic assay



Serum bactericidal assay





Il a progressivement été montré que pour les anticorps anticapsulaires, des tests fonctionnels reflétaient mieux la protection : OPA pour le pneumocoque, SBA pour le méningocoque

Table 2. Correlates of protection for pneumococcal, Hib and meningococcal vaccines.

Vaccines	Correlates of Protection
PCV	ELISA >0.35 µg/mL OPA ≥8 titre
Hib	ELISA Long term: ≥1.0 µg/mL Short term: >0.15 µg/mL SBA ≥4 titre
Meningococcal *	SBA rSBA (≥8 titre) or hSBA (≥4 titre)

OPA : explorer comment les anticorps générés favorisent la phagocytose bactérienne

SBA : explorer comment les anticorps générés favorisent la bactéricidie médiée par le complément

HUMAN IMMUNITY TO THE MENINGOCOCCUS

I. The Role of Humoral Antibodies

By IRVING GOLDSCHNEIDER, M.D., EMIL C. GOTSCHLICH, M.D., and MALCOLM S. ARTENSTEIN, M.D.

(*From The Department of Bacteriology, Walter Reed Army Institute of Research, Washington, D. C. 20012*)

(Received for publication 20 February 1969)

L'équipe de Goldschneider conduit des travaux séminaux dans les années 60 dans des garnisons de jeunes appelés, pour explorer quelle réponse immune protège contre le méningocoque

Pouvoir bactéricide du serum chez les cas avant leur infection …

TABLE III

Reconstitution of Bactericidal Activity of Human Gamma Globulin by Sera from Prospective Cases of Meningococcal Disease*

Sera		Reciprocal bactericidal titer‡	
Description	Code No.	Serum	Serum (1:4) + gamma globulin§
Base line sera from prospective cases of meningococcal disease	2,651	<4	256
	6,884	<4	128
	7,123	<4	32
	8,860	<4	256
	9,587	<4	128
	10,325	<4	128
	10,662	<4	128
	12,059	<4	128
Complement (P. M.)		<4	128

* Base line sera from recruits in 1st wk of training at Fort Dix, N. J., 1967–1968.

‡ Tested against meningococcal strain C11 (serogroup C).

Et *après* leur infection …

TABLE IV

*Bactericidal Activity of Convalescent Sera from Cases of Meningococcal Disease**

Sera		Onset of disease	Reciprocal bactericidal titer‡
Code No.	Date obtained		
A-612	12 April	11 March	1024
A-616	4 April	9 March	512
A-635	23 April	25 March	512
A-637	20 April	22 March	1024
A-640	28 March	28 February	512
A-645	5 April	8 March	2048
A-651	9 April	12 March	1024
A-656	4 April	25 February	1024
A-668	12 April	12 March	1024
A-670	17 April	18 March	512
A-677	6 April	13 March	256

* Fort Dix, N. J., 1968. All cases caused by group C meningococci.

Proportion de personnes avec un titre de bactéricidie du sérum ≥1/4 chez les cas et les contrôles : bien plus élevée chez les contrôles

Meningococcocidal Activity of Base Line Sera from Prospective Cases of Meningococcal Disease*

Meningococci	Bactericidal titer 1:4 or greater		Statistical significance
	Base line sera from cases	Base line sera from controls	
	No. positive/total (%)		
Homologous strains‡	3/54 (5.6)	444/540 (82.2)	$P < 0.001$§
Other pathogenic strains			
A1 (serogroup A)	4/23 (17.4)	166/230 (72.2)	$P < 0.001$‖
B11 (serogroup B)	3/23 (13.0)	179/230 (77.8)	$P < 0.001$‖
C11 (serogroup C)	2/23 (8.7)	154/230 (67.0)	$P < 0.001$‖

* Obtained from recruits in 1st wk of basic training at Fort Dix, N. J., 1967–1968.

HUMAN IMMUNITY TO THE MENINGOCOCCUS

IV. Immunogenicity of Group A and Group C Meningococcal Polysaccharides in Human Volunteers

By EMIL C. GOTSCHLICH, M.D., IRVING GOLDSCHNEIDER, M.D., and MALCOLM S. ARTENSTEIN, M.D.

(*From The Department of Bacteriology, Walter Reed Army Institute of Research, Washington, D. C. 20012*)

(Received for publication 20 February 1969)

La vaccination par le polysaccharide bactérien déclenche un pouvoir bactéricide du sérum

TABLE VII

Serum Bactericidal Antibody in Six Subjects after Immunization with Meningococcal Group-Specific Polysaccharides

Subject	Immunogen	Reciprocal bactericidal titer against			
		Group A strains		Group C strains	
		A1	121 misc.	C11	107 VI
M. S. A.					
5 April	C-5, 5 April	4	4	16	16
12 "		4	4	128	512
19 "	A-5, 19 April	4	4	2048	1024
26 "		32	32	2048	1024
3 May		128	256	2048	1024
13 August		256	256	2048	2048
W. C. B.					
1 April	C-5, 5 April	4	4	8	8
12 "		4	4	16	64
18 "		4	4	128	256
26 "		4	4	128	256
3 May		4	8	128	256
13 August		4	4	128	256
I. G.					
2 April	C-5, 5 April	32	32	16	16
12 "		32	16	32	64
19 "	A-5, 19 April	32	16	256	512
26 "		32	128	256	256
3 May		64	256	256	512
17 May		64	256	256	512
13 August		128	256	256	512
E. C. G.					
30 November	A-2, 30 November	4	8	8	4
7 December		8	16	8	
11 "		64	128		
14 "	C-2, 14 December	64	128	8	4
21 "		64	128	256	256
28 "		64	128	256	512
5 January		64	256	256	512
13 August		128	256	128	512

Complement-Mediated Bactericidal Activity of Human Antibodies to Poly α2→8 *N*-Acetylneuraminic Acid, the Capsular Polysaccharide of *Neisseria meningitidis* Serogroup B

1995

Robert E. Mandrell, Farrukh H. Azmi, and Dan M. Granoff

Children's Hospital Oakland Research Institute, Oakland, California

Des anticorps anti-polysaccharides sont bien porteurs d'une bactéricidie

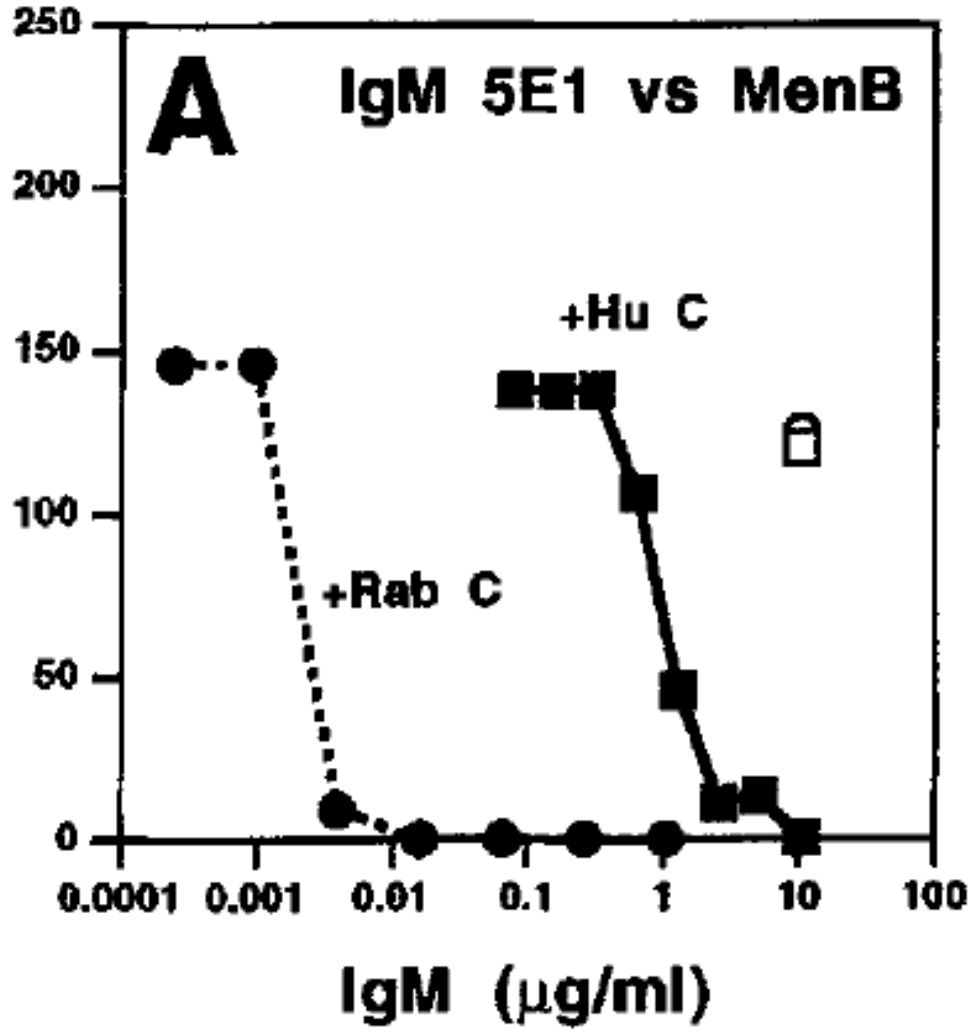


Figure 1. Bactericidal activities of human anti–meningococcal serogroup B (MenB) polysaccharide and anti–*Haemophilus influenzae* type b (Hib) polysaccharide MAbs with human complement (Hu C) or rabbit complement (Rab C).

Relationship between Serum Bactericidal Activity and Serogroup-Specific Immunoglobulin G Concentration for Adults, Toddlers, and Infants Immunized with *Neisseria meningitidis* Serogroup C Vaccines

DANIEL J. SIKKEMA,* KEITH E. FRIEDMAN, BARTHOLOMEW CORSARO, ALAN KIMURA,† STEPHEN W. HILDRETH, DACE V. MADORE, AND SALLY A. QUATAERT

Wyeth-Lederle Vaccines and Pediatrics, West Henrietta, New York 14586

Une corrélation est observée entre mesure Elisa et mesure SBA de la réponse vaccinale …

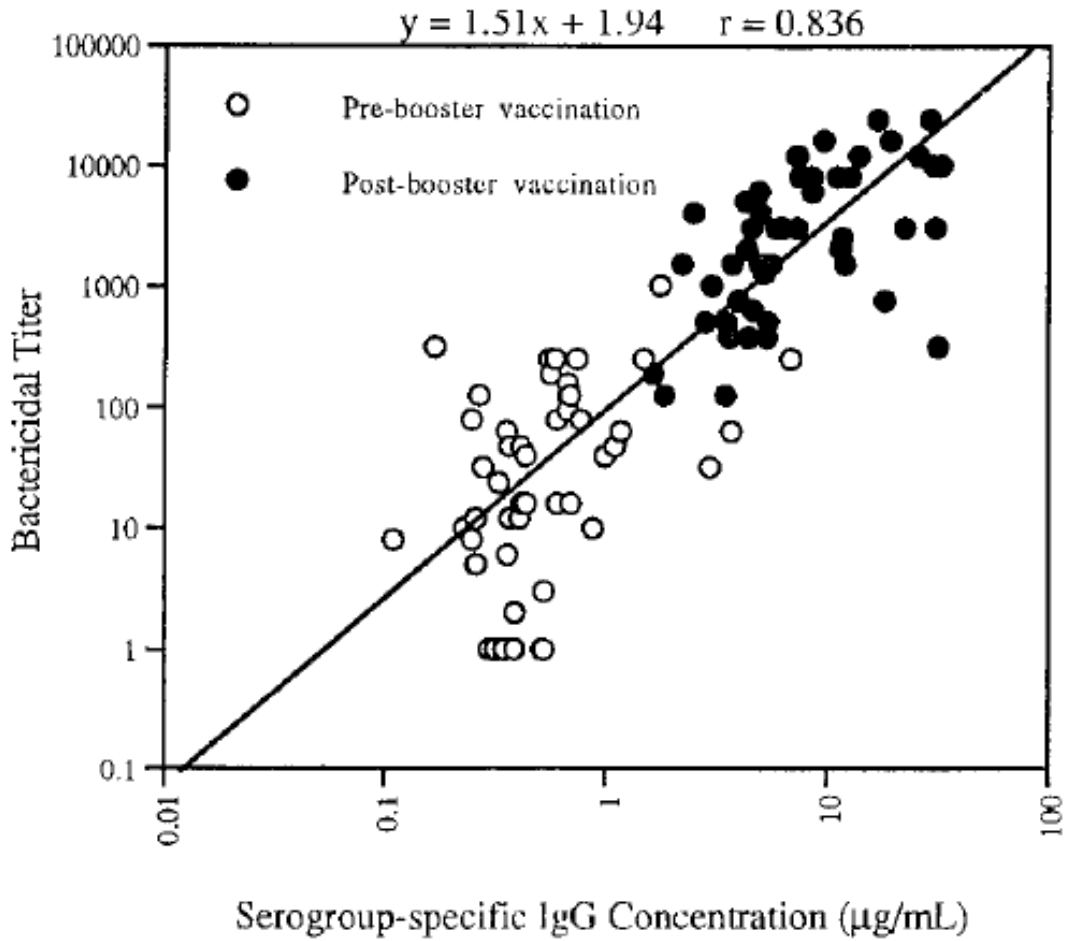


FIG. 3. Correlation between *N. meningitidis* serogroup-specific IgG concentration and serum bactericidal titer. Sera were collected prior to and approximately 30 days after administration of a fourth immunization dose (booster dose given at 12 to 15 months of age) to toddlers, following completion of a primary immunization series as infants (immunized at 2, 4, and 6 months of age). Forty-eight pre- and postimmunization sera were analyzed.

CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, Sept. 2000, p. 764–768
1071-412X/00/$04.00+0

INFECTION AND IMMUNITY, June 1998, p. 2453–2459 Vol. 66, No. 6
0019-9567/98/$04.00+0

Age-Dependent *Neisseria meningitidis* Serogroup C Class-Specific Antibody Concentrations and Bactericidal Titers in Sera from Young Children from Montana Immunized with a Licensed Polysaccharide Vaccine

SUSAN E. MASLANKA,[1]* JORDAN W. TAPPERO,[1] BRIAN D. PLIKAYTIS,[1] ROBERT S. BRUMBERG,[1]† JANET K. DYKES,[1] LINDA L. GHEESLING,[1] KIMBERLEY B. J. DONALDSON,[1] ANNE SCHUCHAT,[1] JOHN PULLMAN,[2] MARYANN JONES,[2] JULIE BUSHMAKER,[2] AND GEORGE M. CARLONE[1]

Mais cette corrélation n'est pas présente chez les nourrissons pour le vaccin non conjugué

TABLE 1. Age-dependent meningococcal serogroup C total and class-specific ELISA antibody concentrations

Immunization status	Antibody class	Antibody concn (μg/ml)[a] in:					
		1-yr-olds (n = 55)	2-yr-olds (n = 31)	3-yr-olds (n = 36)	4-yr-olds (n = 32)	5-yr-olds (n = 19)	Adults (n = 40)
Preimmunization	Total	0.43 (0.30–0.61)	0.32 (0.18–0.57)	0.37 (0.25–0.55)	0.38 (0.26–0.56)	0.41 (0.27–0.62)	1.01 (0.68–1.48)
Postimmunization (6 wk)	Total	4.61 (3.80–5.61)	6.19 (4.64–8.25)	8.90 (6.04–13.13)	8.47 (6.25–11.48)	6.24 (3.85–10.11)	33.24 (23.55–46.90)
	IgG	3.64 (2.96–4.49)	4.58 (3.52–5.97)	6.62 (4.37–10.04)	5.67 (3.98–8.08)	4.16 (2.36–7.32)	17.74 (11.54–27.26)
	IgM	0.27 (0.23–0.31)	0.29 (0.21–0.41)	0.42 (0.30–0.59)	0.67 (0.46–0.96)	0.54 (0.37–0.78)	3.45 (2.56–4.65)
	IgA	0.39 (0.28–0.54)	0.57 (0.27–1.20)	1.09 (0.61–1.94)	1.32 (0.94–1.85)	1.19 (0.77–1.86)	6.23 (4.25–9.12)

[a] Geometric mean $\log_2$ antibody concentrations, with 95% confidence limits in parentheses.

Elisa

TABLE 2. Age-dependent meningococcal serogroup C bactericidal titers

Immunization status	Titer[a] in:					
	1-yr-olds (n = 55)	2-yr-olds (n = 31)	3-yr-olds (n = 36)	4-yr-olds (n = 32)	5-yr-olds (n = 19)	Adults (n = 40)
Preimmunization	4.0 (—[b])	4.3 (3.9–4.7)	4.1 (3.9–4.2)	4.0 (—)	4.2 (3.9–4.5)	9.0 (5.22–15.62)
Postimmunization (6 wk)	7.2 (5.0–10.4)	11.7 (6.0–20.5)	38.1 (17.5–83.0)	72.9 (34.1–155.9)	44.4 (14.6–135.6)	2,521.4 (1,450.5–4,383.0)

[a] Geometric mean $\log_2$ reciprocal titers, with 95% confidence intervals in parentheses.
[b] —, no variability about the mean; all were <1:8.

SBA

L’OMS recommande d’évaluer par le SBA les vaccins anti-méningocoque

The Immunological Basis for Immunization Series

Module 15: Meningococcal disease Updated 2020

Available online at www.sciencedirect.com
ScienceDirect
Vaccine 25 (2007) 3816–3826
Vaccine
www.elsevier.com/locate/vaccine

Estimating the protective concentration of anti-pneumococcal capsular polysaccharide antibodies

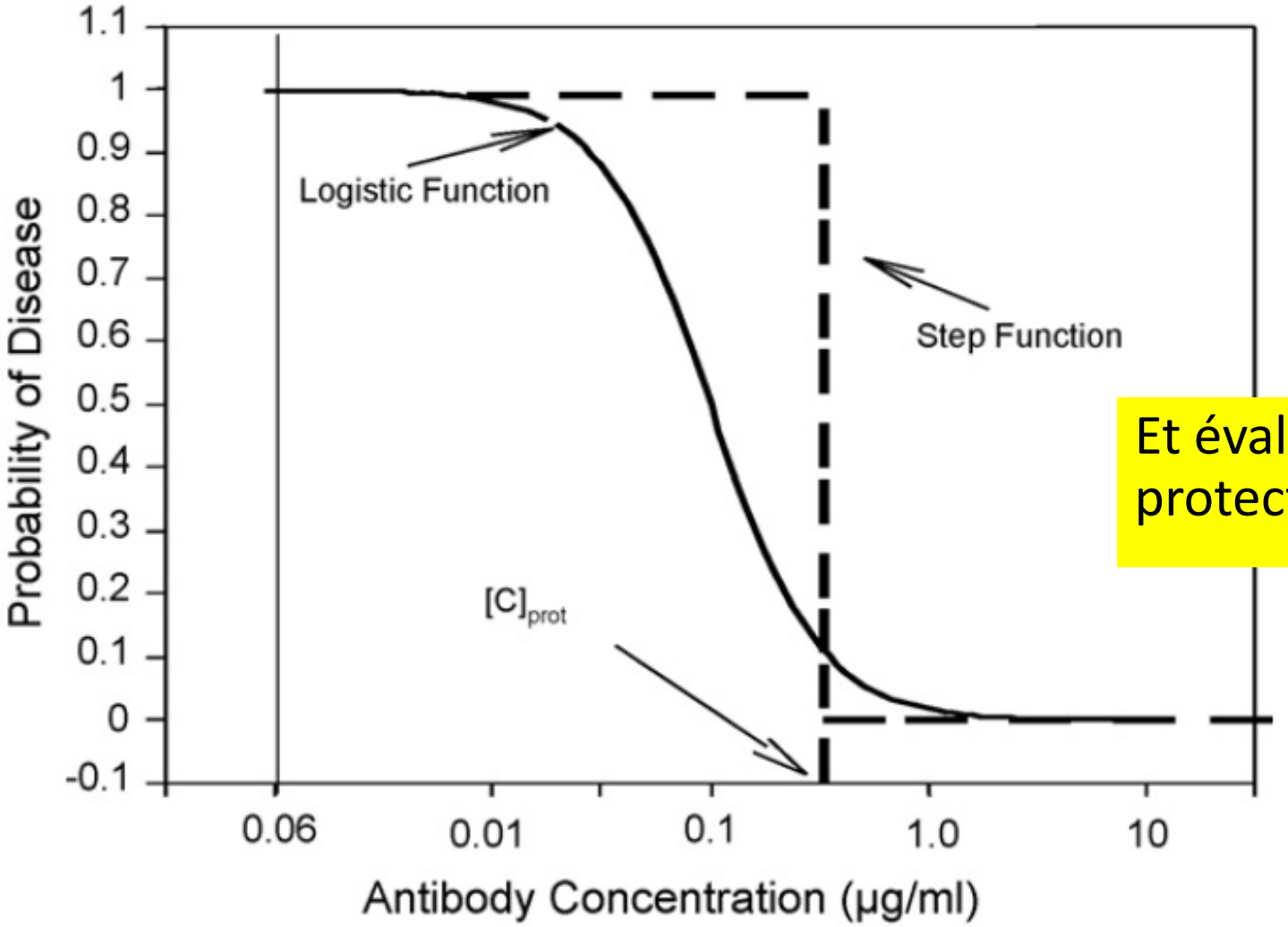
George R. Siber[a,*], Ih Chang[b], Sherryl Baker[a], Philip Fernsten[a], Katherine L. O'Brien[c], Mathuram Santosham[c], Keith P. Klugman[d,e], Shabir A. Madhi[e], Peter Paradiso[a], Robert Kohberger[f]

Le test fonctionnel le plus utilisé pour le pneumocoque est l'OPA ; cette étude explore le lien entre protection et OPA lors de 3 essais cliniques …

Table 1
Three controlled double blind efficacy trials of pneumococcal conjugate vaccine used in meta-analysis of protective pneumococcal antibody concentration

	Evaluable patients (per protocol)		IPD Cases (7vPnC types, per protocol)		Efficacy (95% CI)	No. of sera assayed by single absorption ELISA with C-Ps	
Study/Author	Control	PnC	Control	PnC		Control	PnC
NCKP (2000) Black et al. [6]	10,995 (MnCC)	10,940 (7vPnC)	39	1	**97.4%** (82.7, 99.9)	189 (180)[a]	190 (188)[a]
American Indian (2003) O'Brien et al. [7]	2818 (MnCC)	2974 (7vPnC)	8	2	**76.8%** (−9.4, 95.1)	481	445
South Africa (2003) Klugman et al. [8]	18,550 (Placebo)	18,557 (9vPnC)	10	1	**90%** (29.7, 99.8)[b]	302	256
Pooled studies	33,363	32,471	57	4	**93.0%** (81, 98.2)	972	891

The bold number is Geometric Mean followed by 95% CI (GM is bold, 95% CI).
[a] No. of sera re-assayed by double absorption ELISA with both C-Ps and type 22F Ps.
[b] Efficacy for the 7 serotypes in Prevnar in non-HIV infected children [8].



Et évalue à 0,35 µg/mL le taux protecteur

Fig. 1. Theoretical relationship between risk of disease and concentration of protective antibodies. The step function represents the simplifying assumption required to calculate a protective concentration, $[C]_{prot}$.

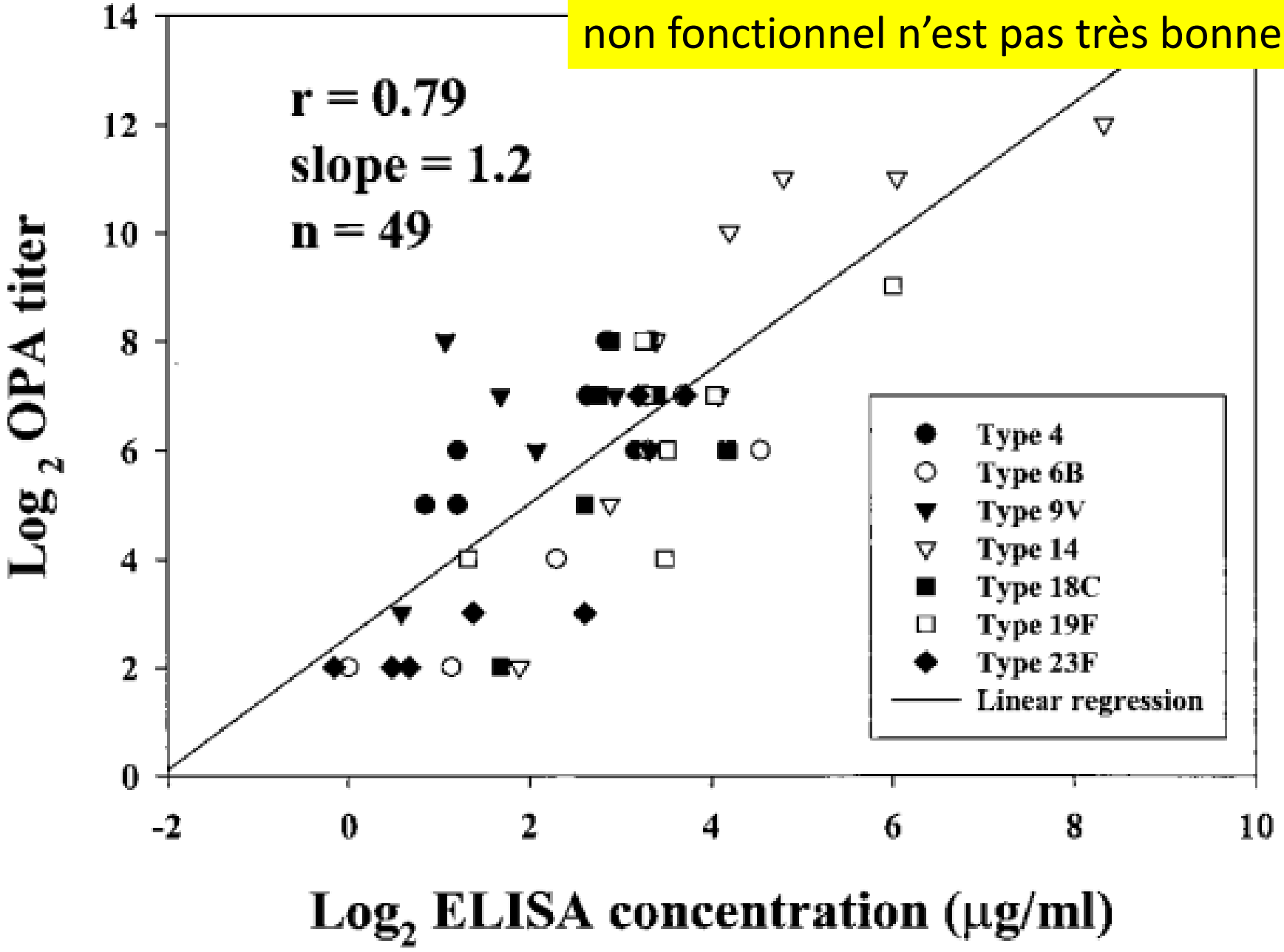
CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, Nov. 2003, p. 1019–1024
1071-412X/03/$08.00+0 DOI: 10.1128/CDLI.10.6.1019–1024.2003

Vol. 10, No. 6

Multilaboratory Evaluation of a Viability Assay for Measurement of Opsonophagocytic Antibodies Specific to the Capsular Polysaccharides of *Streptococcus pneumoniae*

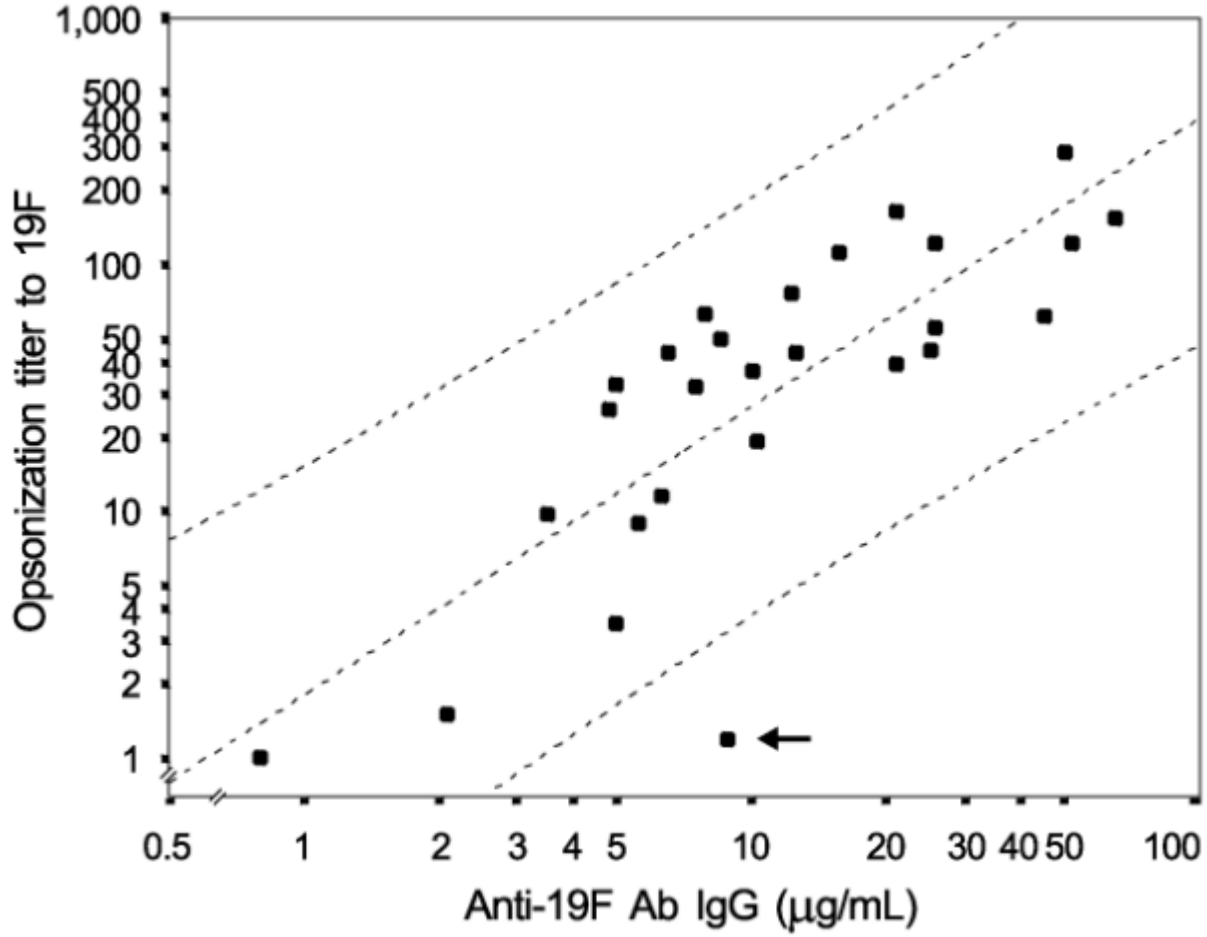
Sandra Romero-Steiner,[1]* Carl Frasch,[2] Nelydia Concepcion,[2] David Goldblatt,[3] Helena Käyhty,[4] Merja Väkeväinen,[4]† Craig Laferriere,[5] Dominique Wauters,[5] Moon H. Nahm,[6] Mark F. Schinsky,[1]‡ Brian D. Plikaytis,[1] and George M. Carlone[1]

La corrélation entre test fonctionnel et non fonctionnel n'est pas très bonne



J Korean Med Sci 1999; 14: 475-9
ISSN 1011-8934

Evaluation of Antibody Responses to Pneumococcal Vaccines with ELISA and Opsonophagocytic Assay



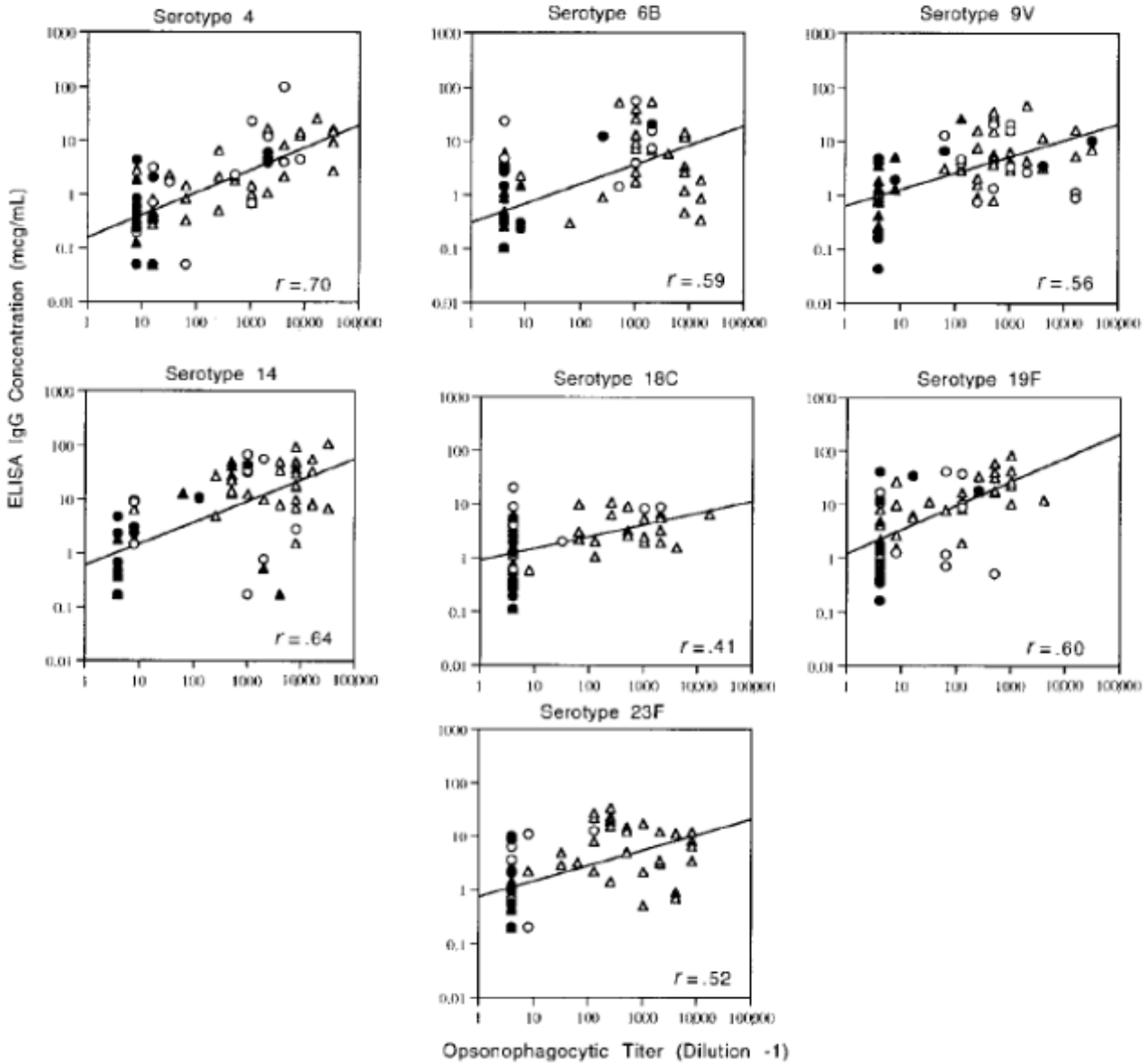
Comparison of an Opsonophagocytic Assay and IgG ELISA to Assess Responses to Pneumococcal Polysaccharide and Pneumococcal Conjugate Vaccines in Children and Young Adults with Sickle Cell Disease

2000

L. Vernacchio,[1,2] S. Romero-Steiner,[3] J. E. Martinez,[3]
K. MacDonald,[1] S. Barnard,[3] T. Pilishvili,[3]
G. M. Carlone,[3] D. M. Ambrosino,[1] and D. C. Molrine[1]

ELISA

OPA



Annex 3

Recommendations to assure the quality, safety and efficacy of pneumococcal conjugate vaccines

Replacement of WHO Technical Report Series, No. 927, Annex 2

L'OMS recommande l'OPA pour évaluer les vaccins contre le pneumocoque

C.2 Assessment of immune responses

C.2.1 Assays to assess serotype-specific antibody responses

Immune responses to pneumococcal conjugate vaccines can be assessed by:

- Determination of serotype-specific IgG antibody geometric mean concentrations (GMCs) based on measurement of binding to polysaccharides (e.g. using an ELISA method). Appendix 1 provides a detailed consideration of the development and standardization of ELISA methods, including:
  - alternative methods to ELISA for measurement of serotype-specific IgG concentrations;
  - the need to use a reference standard and quality control (QC) sera for IgG assays;
  - the need to bridge new assays (whether ELISA or not) to the WHO reference assay and the option of deriving alternative threshold values when using new assays that correspond to 0.35 µg/ml based on a well-justified rationale.
- Determination of serotype-specific functional antibody titres using an OPA (*49*). The conduct of OPAs is addressed in Appendix 1.

Virus

Infections virales

- Les corrélats de protection les plus évidents sont les anticorps neutralisants quant à **l'acquisition** de l'infection
  - Anti-HBs
  - Anti-spike des coronavirus
  - Anti-protéine de fusion du VRS
  - Anti-glycoprotéine d'enveloppe pour Ebola
  - Anti-capside pour le chikungunya
- Les anticorps non neutralisants peuvent cependant être protecteurs
- Problématique à part : le **contrôle** d'une infection latente
  - L'immunité cellulaire est théoriquement plus pertinente
  - Zona

vaccines

MDPI

Systematic Review

Immunogenicity of Recombinant Zoster Vaccine: A Systematic Review, Meta-Analysis, and Meta-Regression

Lorenzo Losa [1,†], Ippazio Cosimo Antonazzo [1,2,†], Giuseppe Di Martino [3,4], Giampiero Mazzaglia [1], Silvio Tafuri [5], Lorenzo Giovanni Mantovani [1,2,‡] and Pietro Ferrara [1,2,*,‡]

L'immunité cellulaire générée par le vaccin subunitaire zona a été très étudiée, et elle est considérée comme plus pertinente que la réponse immune …

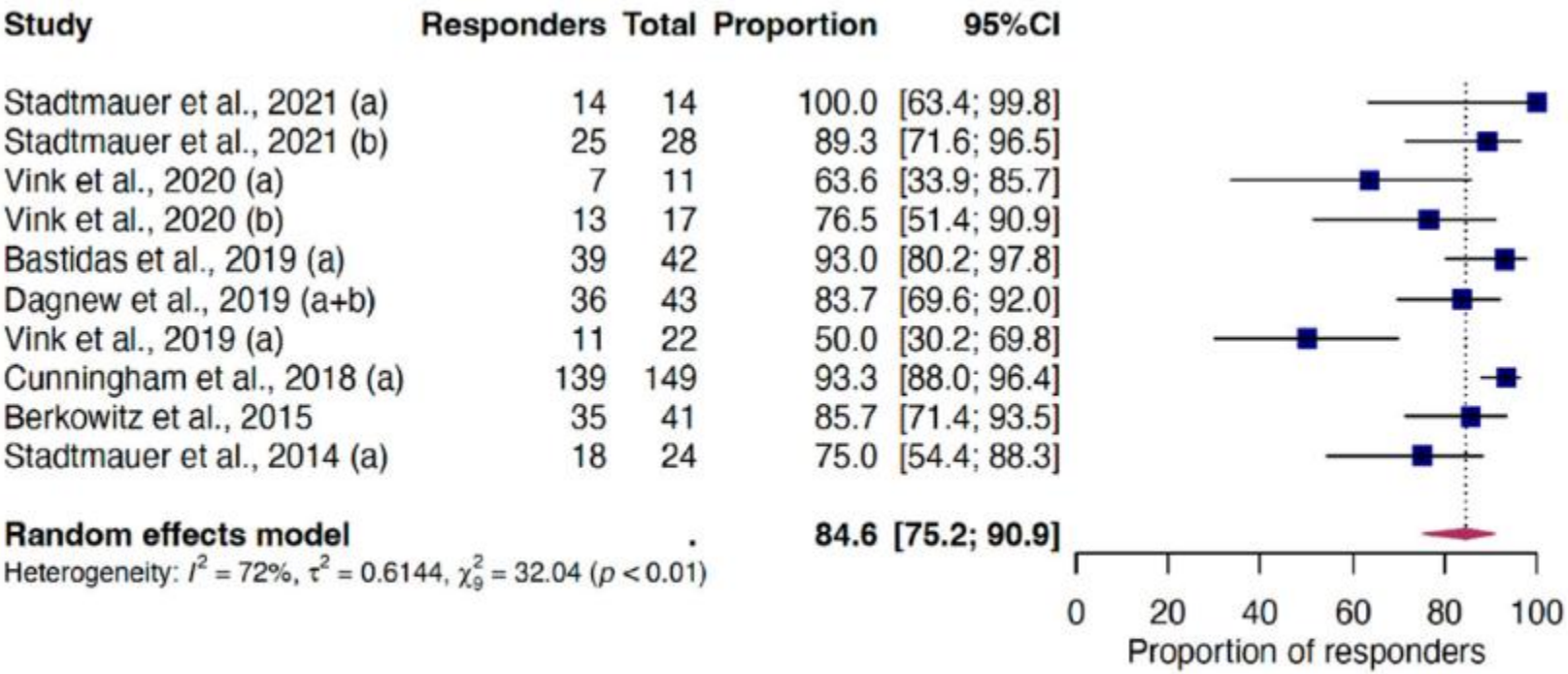


Figure 4. Random-effect meta-analysis of the VRR for cell-mediated immunity one month following

Mais l'immunité humorale a aussi été très étudiée, sans qu'il y ait beaucoup d'arguments pour penser qu'elle joue un rôle.

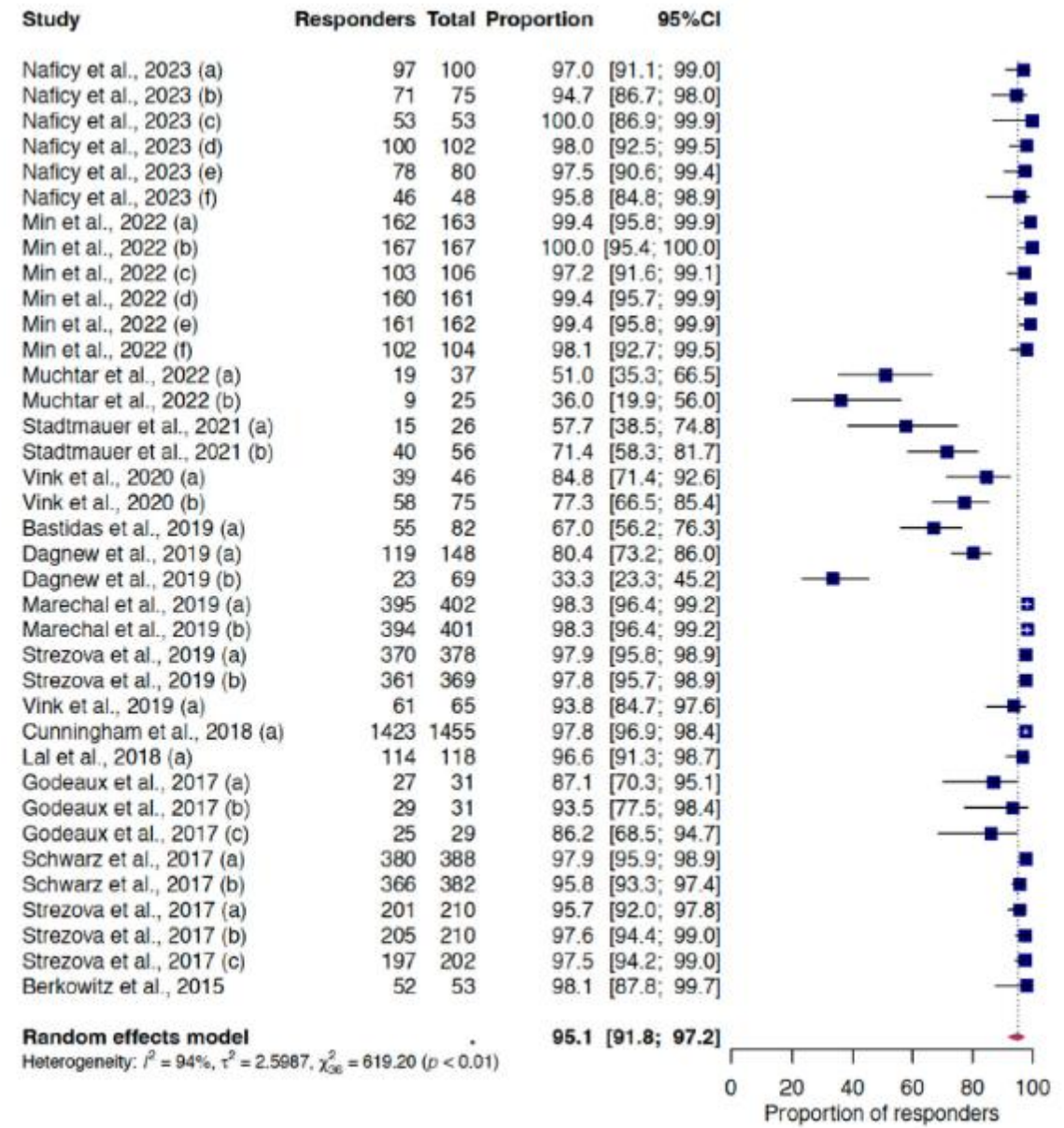


Figure 2. Random-effect meta-analysis of the VRR for humoral immunity one month following RZV-dose 2.

The Journal of Infectious Diseases

BRIEF REPORT

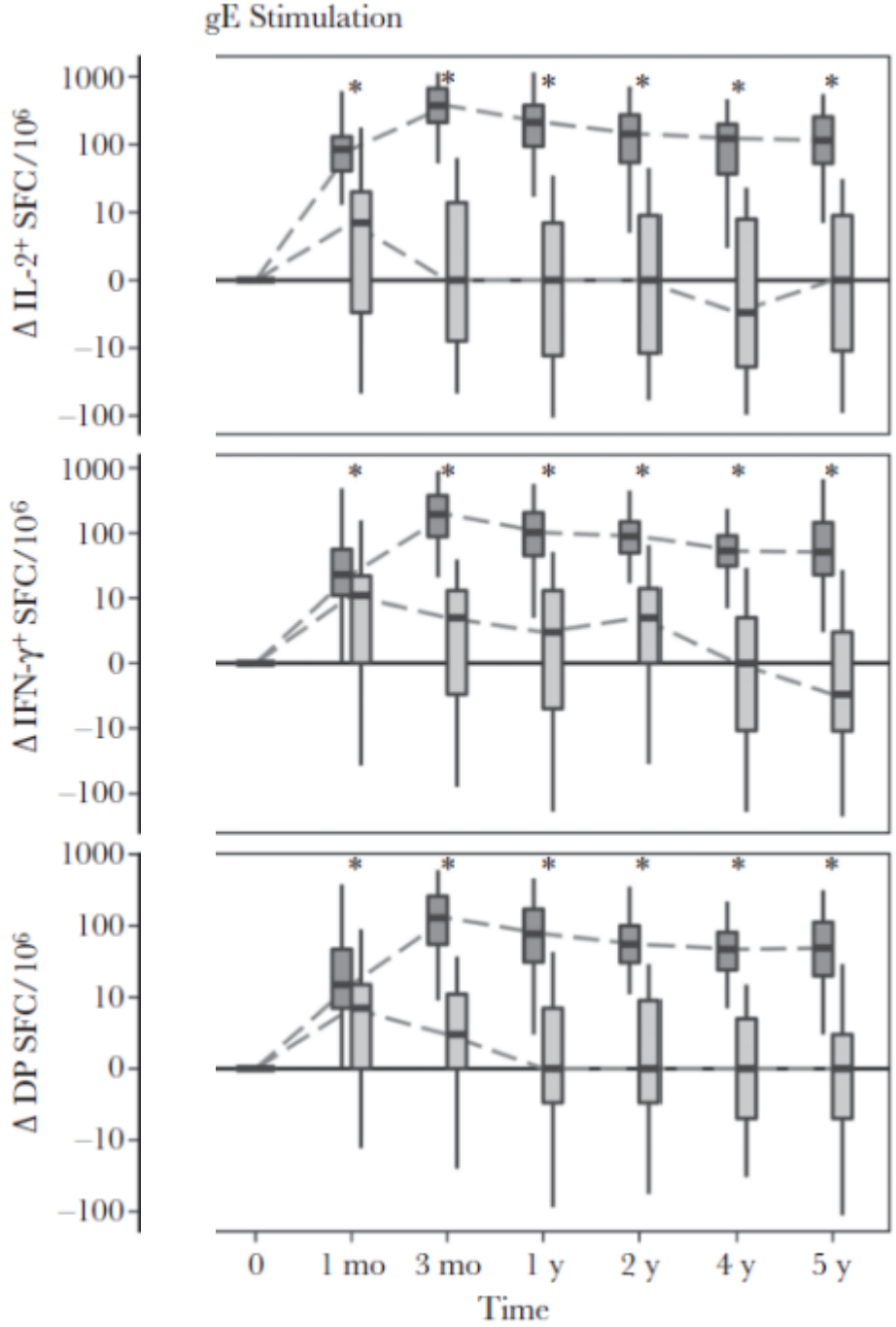
Cell-Mediated Immune Responses After Administration of the Live or the Recombinant Zoster Vaccine: 5-Year Persistence

Michael J. Johnson,[1] Cuining Liu,[2] Debashis Ghosh,[2] Nancy Lang,[1] Myron J. Levin,[1] and Adriana Weinberg[1]

[1]University of Colorado School of Medicine, Aurora, Colorado, USA, and [2]Colorado School of Public Health, Aurora, Colorado, USA

Vaccine RZV ZVL

Le vaccin subunitaire a une efficacité plus longue que le vaccin vivant ; la réponse cellulaire à long terme est également meilleure ; est-ce un argument pour dire qu'elle est plus proche d'un CoP ?



Open Forum Infectious Diseases

BRIEF REPORT

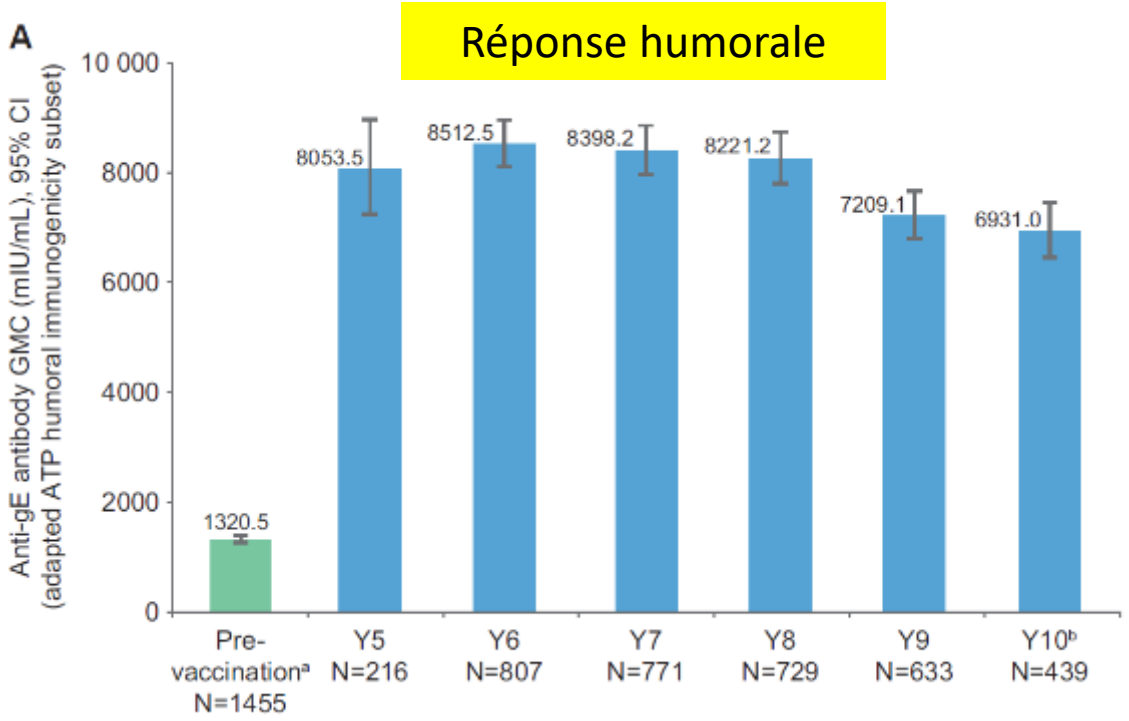
Long-term Protection Against Herpes Zoster by the Adjuvanted Recombinant Zoster Vaccine: Interim Efficacy, Immunogenicity, and Safety Results up to 10 Years After Initial Vaccination

Ana Strezova,[1] Javier Diez-Domingo,[2] Kamal Al Shawafi,[3] Juan Carlos Tinoco,[4] Meng Shi,[5] Paola Pirrotta,[6] and Agnes Mwakingwe-Omari[5] on behalf of the Zoster-049 Study Group[a]

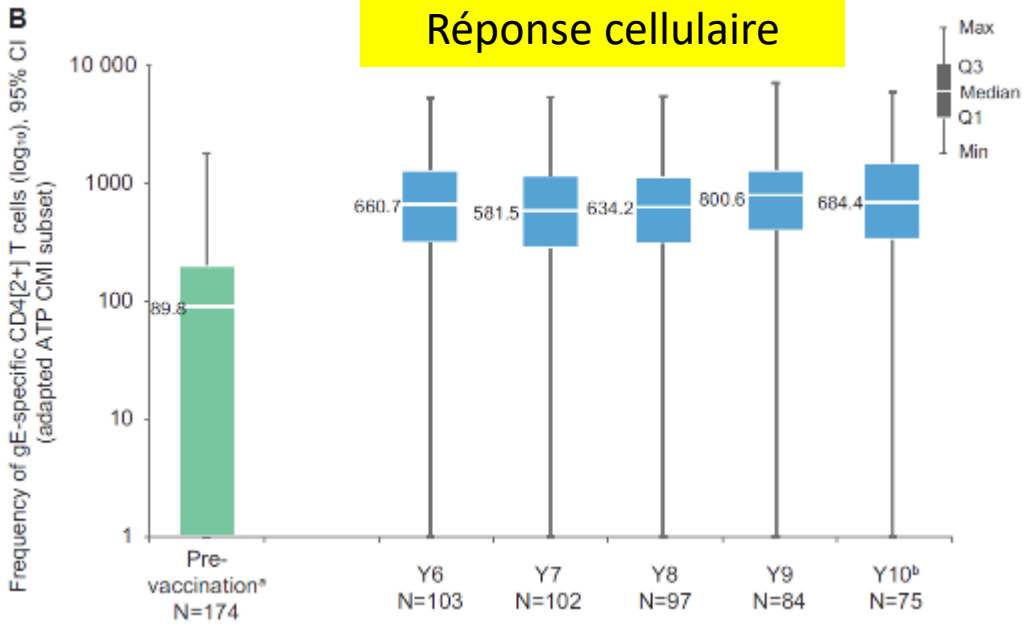
[1]GSK, Rixensart, Belgium, [2]FISABIO Fundación para el Fomento Investigación Sanitaria y Biomédica de la Comunitat Valenciana, Valencia, Spain, [3]Modis, Belgium c/o GSK, Wavre, Belgium, [4]Hospital General de Durango, Durango, Mexico, [5]GSK, Rockville, Maryland, USA, and [6]GSK, Wavre, Belgium

Cet argument ne porte pas, car la réponse humorale également est meilleure avec le vaccin subunitaire

Réponse humorale



Réponse cellulaire



nature medicine

ARTICLES

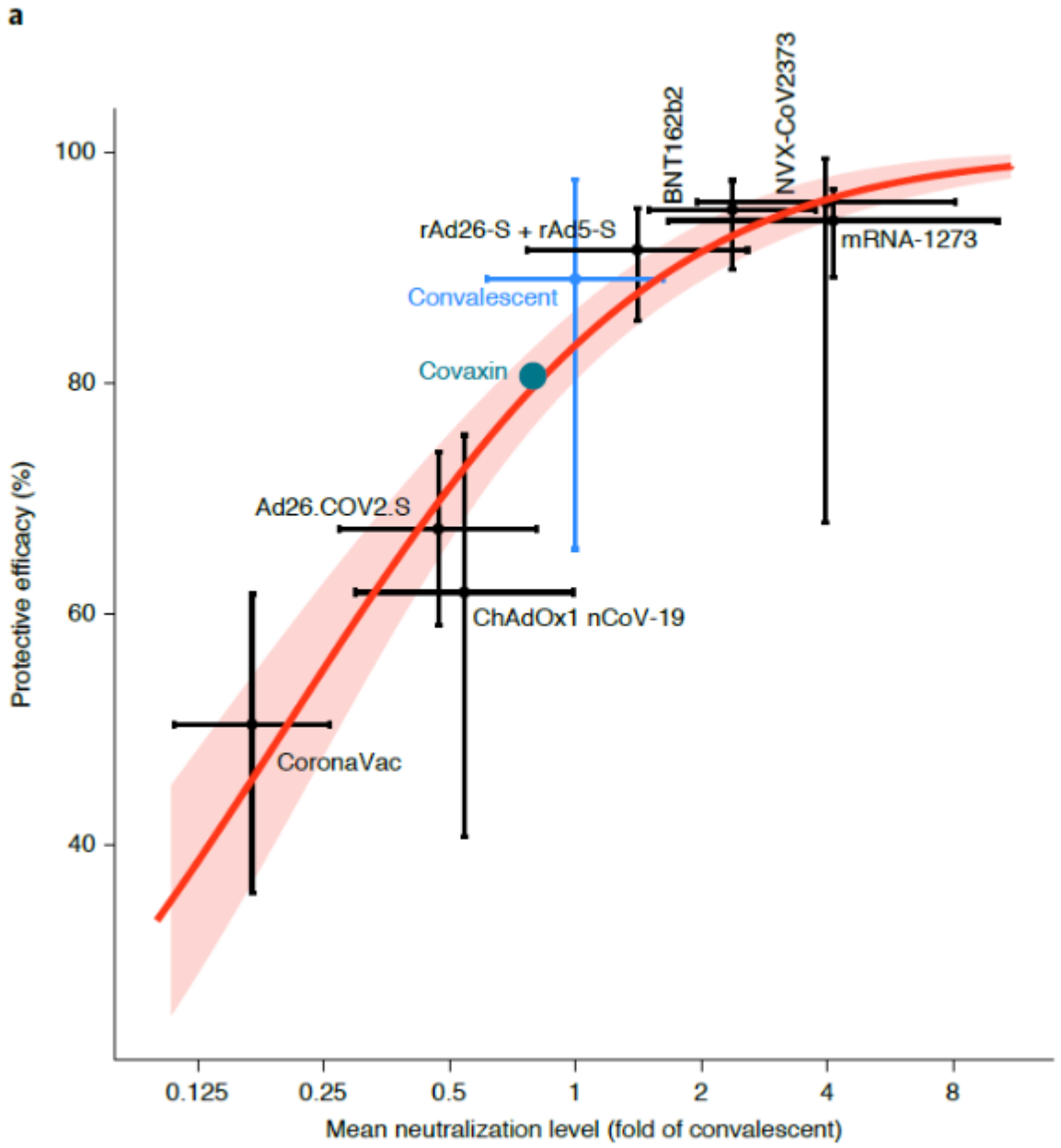
https://doi.org/10.1038/s41591-021-01377-8

Check for updates

Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection

2021

David S. Khoury[1,9], Deborah Cromer[1,9], Arnold Reynaldi[1], Timothy E. Schlub[1,2], Adam K. Wheatley[3], Jennifer A. Juno[3], Kanta Subbarao[3,4], Stephen J. Kent[3,5,6], James A. Triccas[7,8] ✉ and Miles P. Davenport[1] ✉

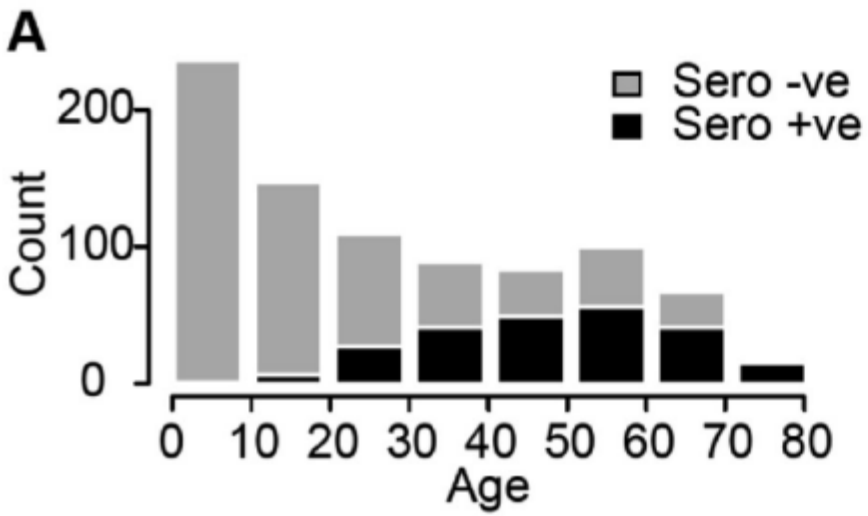


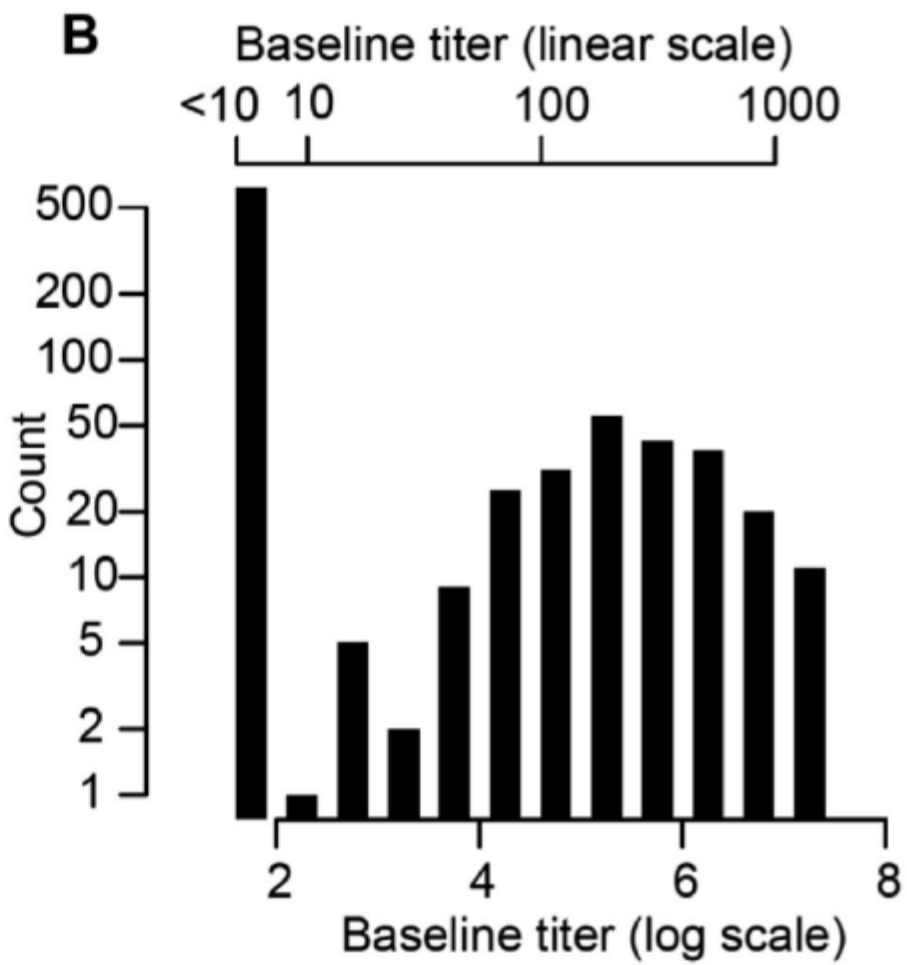
Pour le SARS-CoV-2, les CoP ont pu être établis avant l'apparition des variants, même si ces CoP varient en fonction de ce contre quoi on souhaite protéger : infection, maladie, maladie grave ?

Pre-existing chikungunya virus neutralizing antibodies correlate with risk of symptomatic infection and subclinical seroconversion in a Philippine cohort

2020

In-Kyu Yoon[a,*], Anon Srikiatkhachorn[b,c], Maria Theresa Alera[d], Stefan Fernandez[e], Derek A.T. Cummings[f], Henrik Salje[g]





Une méthode très élégante (et très lourde) a été utilisée pour le chikungunya : on caractérise le taux d'anticorps neutralisant chez plusieurs centaines de personnes avant qu'une épidémie ne survienne (beaucoup ont déjà une telle réponse, du fait de vagues épidémiques antérieures), puis on regarde qui parmi elle fait une infection

Et on peut ainsi déterminer quel taux est associé à une absence d'infection

Table 1
Symptomatic CHIKV infections and subclinical seroconversions among cohort participants with available CHIKV PRNT data from both pre- and post-year visits for the relevant study year (PRNT80 and PRNT50 titers are shown).

Neutralizing antibody titer range		Year 1			Year 2		
		Number in titer group at baseline	Number of chikungunya cases (% of titer group)	Number of subclinical seroconversions with ≥8-fold increase (% of titer group)	Number in titer group at 12 months	Number of chikungunya cases (% of titer group)	Number of subclinical seroconversions with ≥8-fold increase (% of titer group)
PRNT80							
<1:10		615	19 (3.1%)	89 (14.5%)	444	6 (1.4%)	15 (3.4%)
Low (1:10 to <1:100)		48	0	1 (2.1%)	46	0	0
Medium (1:100 to 1:500)	1:100–1:199	53	0	0	60	0	0
	1:200–1:299	47	0	0	50	0	0
	1:300–1:399	20	0	0	35	0	0
	1:400–1:500	19	0	0	40	0	0
High (>1:500)		52	0	0	90	0	0

JCI insight

RESEARCH ARTICLE

2022

Effectiveness of CHIKV vaccine VLA1553 demonstrated by passive transfer of human sera

Pierre Roques,[1] Andrea Fritzer,[2] Nathalie Dereuddre-Bosquet,[1] Nina Wressnigg,[2] Romana Hochreiter,[2] Laetitia Bossevot,[1] Quentin Pascal,[1] Fabienne Guehenneux,[3] Annegret Bitzer,[2] Irena Corbic Ramljak,[2] Roger Le Grand,[1] Urban Lundberg,[2] and Andreas Meinke[2]

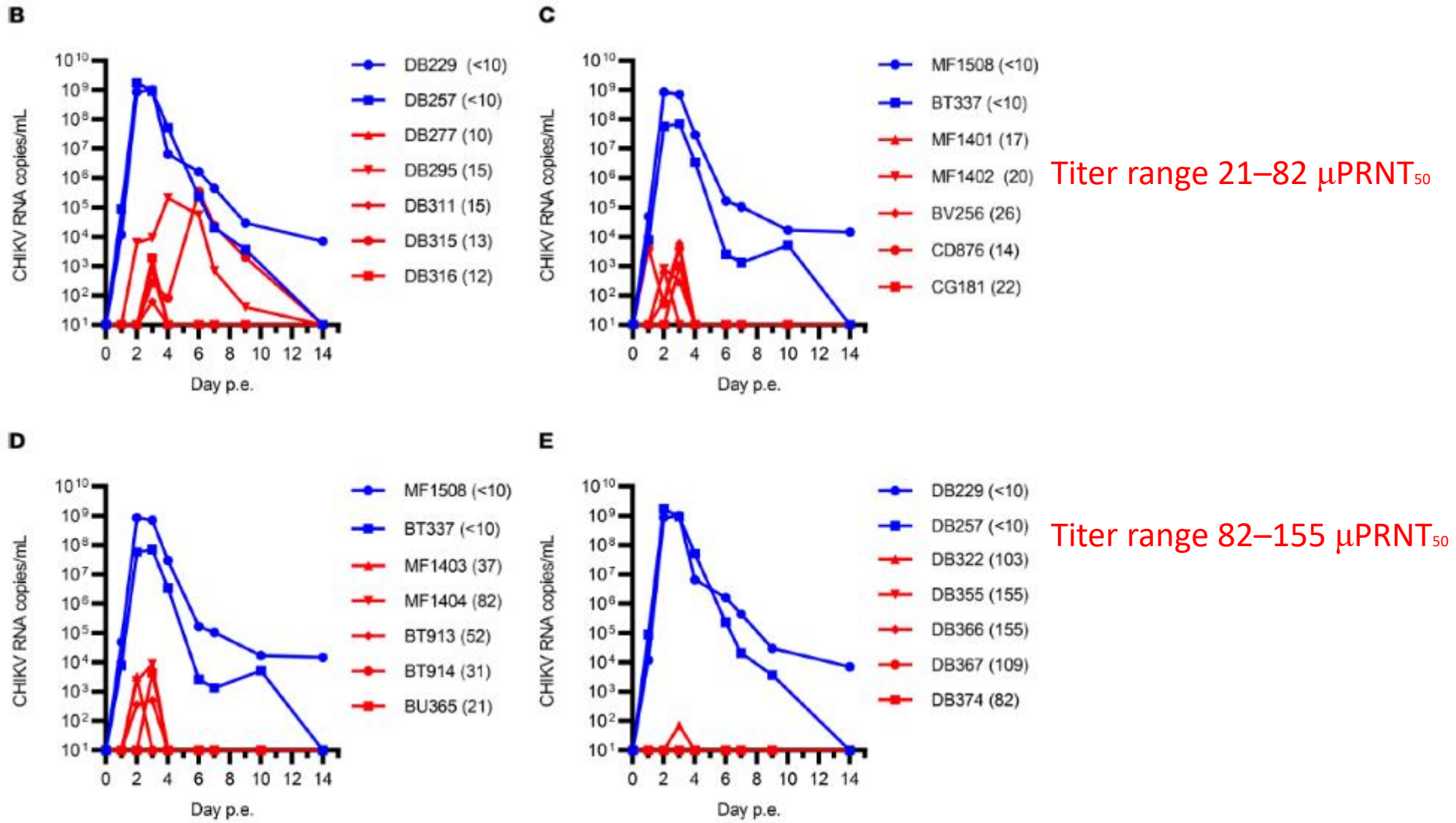
- Vaccination par le candidat-vaccin chikungunya de volontaires sains
  - Réponses immunitaires de différents niveaux
- Prélèvement de leur plasma et injection aux primates non humains
- Puis challenge viral
  - Et corrélation du taux d'anticorps dans le plasma avec la virémie observée

Titer range 10–15 µPRNT$_{50}$

Titer range 14–26 µPRNT$_{50}$

Titer range <10 µPRNT$_{50}$

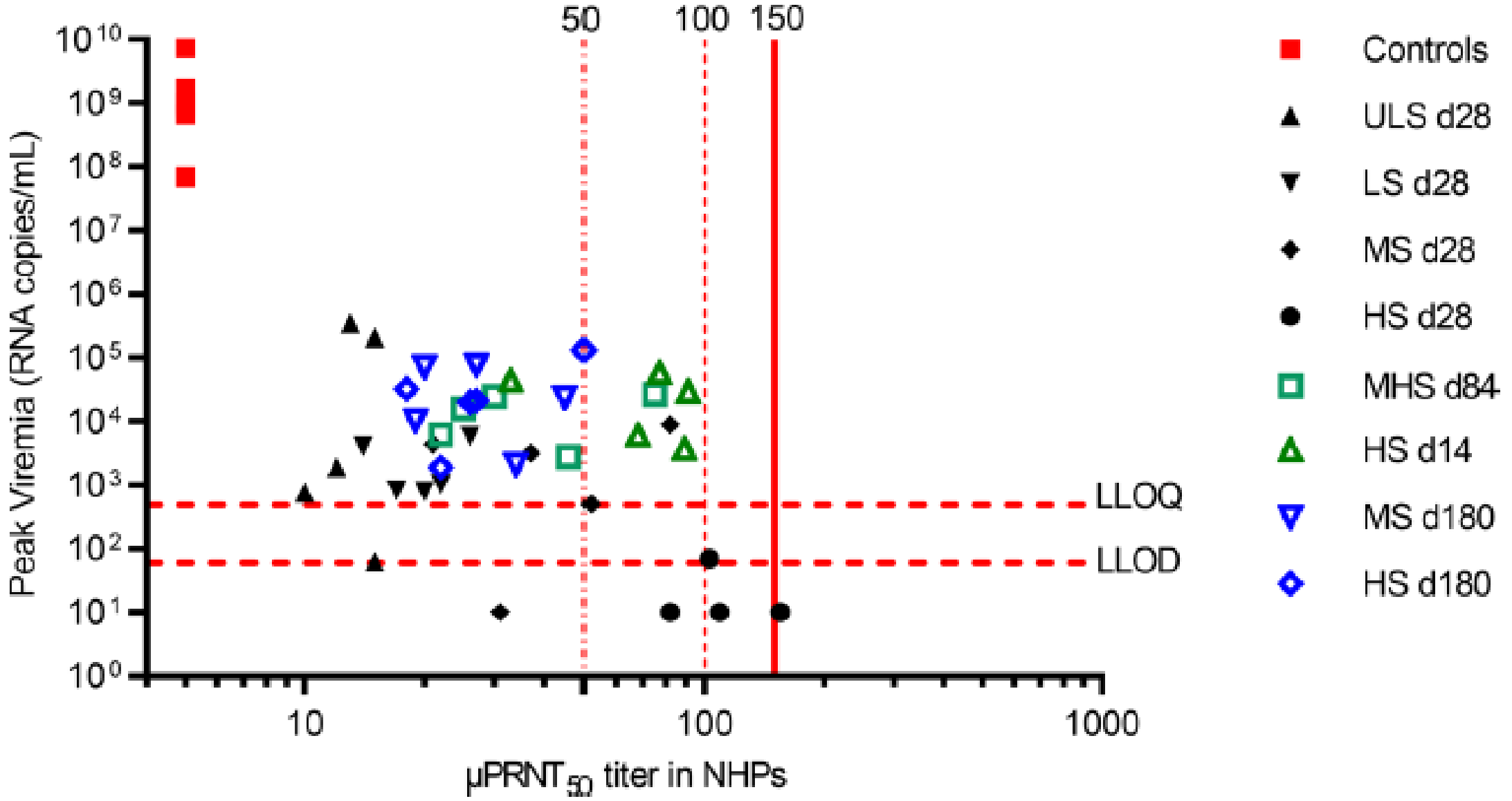
La virémie est d'autant plus faible et courte que les anticorps transférés sont à un taux élevé



Titer range 21–82 µPRNT$_{50}$

Titer range 82–155 µPRNT$_{50}$

Figure 2. Viremia in plasma measured by qPCR. (**A**) Data represent mean viremia ± SEM per VLA1553 phase I serum treatment group and control animals. Viremia magnitude was significantly reduced ($P < 0.001$; repeated-measures 2-way ANOVA, mixed-effects analysis of log transformed data). (**B**–**E**) Viremia in individual animals showing viral load as determined after transfer of ULS d28 (titer range 10–15 µPRNT$_{50}$) (**B**), LS d28 (titer range 14–26 µPRNT$_{50}$) (**C**), MS d28 (titer range 21–82 µPRNT$_{50}$ (**D**), and HS d28 (titer range 82–155 µPRNT$_{50}$) (**E**). Control animals DB229 and DB257 are the same in **B** and **E**; control animals MF1508 and BT337 are the same in **C** and **D**. Control animals receiving nonimmune sera (<10 µPRNT$_{50}$) are shown in blue; VLA1553-specific serum treated animals are shown in red. µPRNT$_{50}$ titer prior to WT CHIKV exposure for the individual animal is shown in brackets. Plasma from d1 to d3 in **C** and **D** and from d1 and 2 in **B** and **E** were tested by classical qPCR (LLOQ, 5000 copies/mL [62.5 copies/rxn]; LLOD, 720 copies/mL [9 copies/rxn]). Samples from all other time points were tested by ultrasensitive qPCR (LLOQ, 500 CHIKV RNA copies/mL [42 copies/rxn]; LLOD, 60 CHIKV RNA copies/mL [5 copies/rxn]). p.e., postexposure.


50
100
150
10^{10}
10^{9}
10^{8}
10^{7}
10^{6}
10^{5}
10^{4}
10^{3}
10^{2}
10^{1}
10^{0}
Peak Viremia (RNA copies/mL)
LLOQ
LLOD
10
100
1000
$\mu PRNT_{50}$ titer in NHPs
Controls
ULS d28
LS d28
MS d28
HS d28
MHS d84
HS d14
MS d180
HS d180

Measles Antibody: Reevaluation of Protective Titers

1990

Robert T. Chen, Lauri E. Markowitz, Paul Albrecht, John A. Stewart, Lynne M. Mofenson, Stephen R. Preblud, and Walter A. Orenstein

From the Division of Immunization, Center for Prevention Services, and the Division of Viral Diseases, Center for Infectious Diseases, Centers for Disease Control, Atlanta, Georgia; the Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, Maryland; and the Division of Communicable Disease Control, Massachusetts Department of Public Health, Jamaica Plain

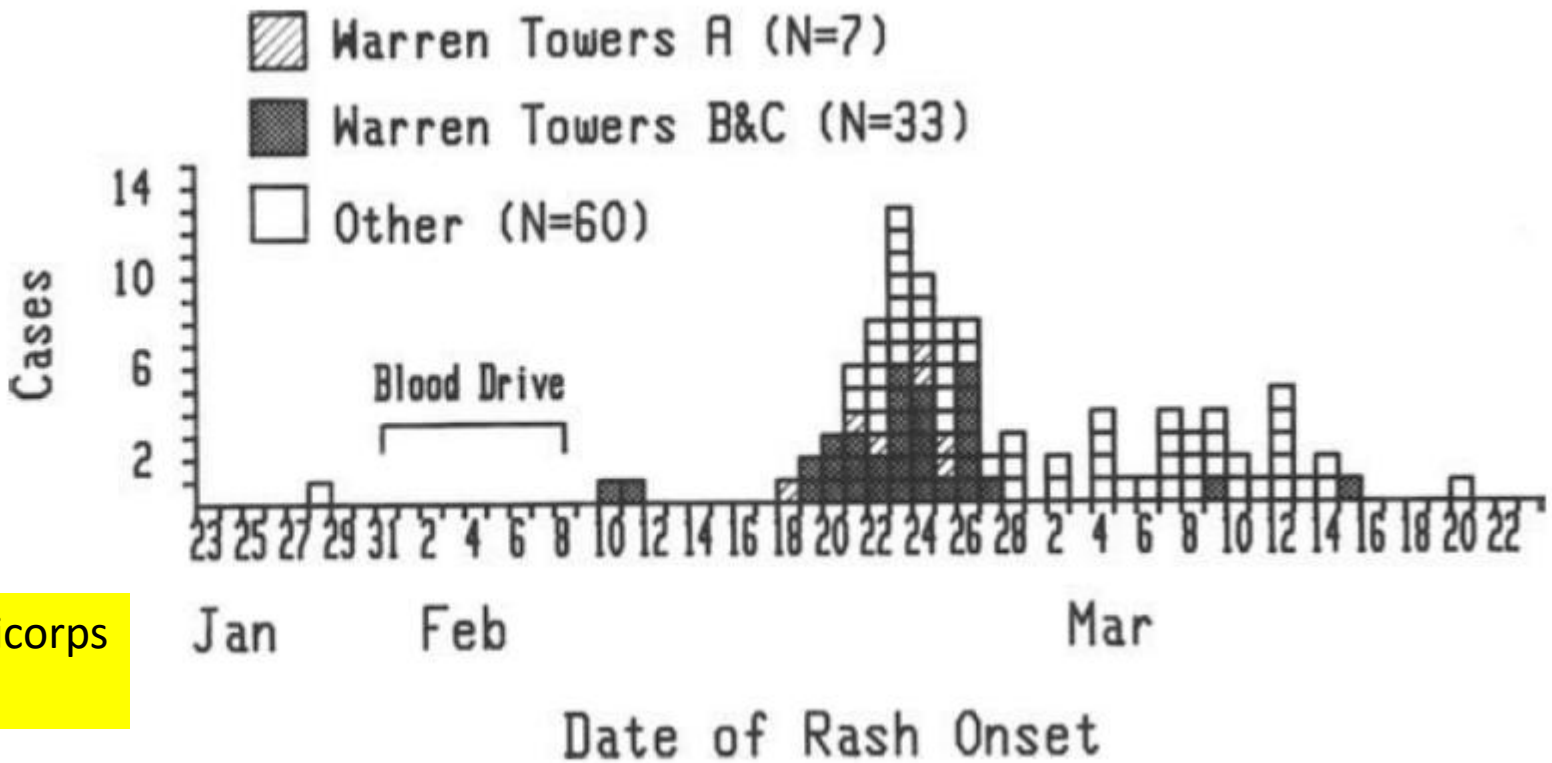


Figure 1. Reported measles cases by date of rash onset, Boston University, 28 January–20 March 1985.

Une autre étude où on regarde le taux d'anticorps (juste !) avant une épidémie

Titres d'anticorps

Cas

Subject(s)	PRN titer: Pre-exposure	PRN titer: Post-exposure	IgM	Fever, days*
Cases				
1	<16	35,363	287	3
2	38	17,723	<160	4
3	80	39,268	102	3
4	86	NA	NA	x
5	86	101,339	<48	4
6	98	44,661	662	3
7	118	14,157	509	3
8	120	13,638	90	2
Total, %				100

… et qui permet d'approcher quel taux d'anticorps est associé à l'infection / à la protection

Non-infectés

Table 2. Prexposure plaque reduction neutralization (PRN) titers and seroconversion, noncases.

Donor	PRN titer: Pre-exposure	PRN titer: Postexposure IgG	PRN titer: Postexposure IgM	Fold titer rise*	Interval (pre- to post-exposure, days)	Age of vaccination†
1	216	1240		6	47	13 mo, 8 y
2	270	9500	<12	35	46	12 mo, 10 y
3	282	370		–	72	12 mo, 11 y
4	286	38,710		133	46	4 y, 11 y
5	390	7520		19	47	(17 y)
6	526	19,400	104	37	96	10 mo, 10 y
7	546	1110	<15	–	78	10 mo, 14 y
8	568	19,400		34	47	10 mo, 8 y
9	620	830		–	47	20 y
10	636	1820	<12	–	46	(12 mo, 11 y)
11	874	31,540	<12	36	46	8 mo, 6 y
12	1052	750		–	46	9 mo, 10 y
13	1076	620		–	95	12 mo, 2 y
14	1988	1220		–	46	(14 mo)
15	2998	1830		–	47	2 y
16	3684	4300		–	47	<6 mo, 10 y
17	3742	1610		–	47	(14 y)
18	5548	1160		–	96	(12 y)

* More than fourfold.
† Provider-verified unless in parentheses.

Temporalité et protection

- Plus la durée d'incubation est courte, plus il est nécessaire que les effecteurs (généralement les anticorps) soient présents à un titre protecteur lors du contage
  - Les rappels sont nécessaires, surtout pour les vaccins non vivants
  - Grippe
  - Méningocoque
  - Tétanos

- Plus la durée d'incubation est longue, plus la protection est possible même après disparition des anticorps
  - La réponse anamnestique prendra de vitesse l'infection
  - Hépatite A, B ; voire rougeole

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PLoS one

Long-Term Protection against HBV Chronic Carriage of Gambian Adolescents Vaccinated in Infancy and Immune Response in HBV Booster Trial in Adolescence

2007

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Table 2. Vaccine efficacy against infection (anti-HBc positive) and chronic carriage (HBsAg positive) among 15 year old Gambians, according to hepatitis B infant vaccination status.

	Fully vaccinated	Partially vaccinated	Unvaccinated
Infection (n/N, % 95% CI)	87/492 (17.7%, 14.4–21.3)	19/84 (22.6%, 14.2–33.0)	226/424 (53.3%, 48.4–58.1)
VE (95% CI)	67.0 (58.2–74.6)	57.7 (37.2–76.8)	Ref
Chronic carriage (n/N, % 95% CI)	2/492 (0.4%, 0.04–1.5)	1/84 (1.2%, 0.03–6.5)	51/420 * (13.2%, 10.1–16.8)
VE (95% CI)	96.6 (91.5–100)	90.1 (69.9–100)	ref

Efficacité vaccinale (surtout contre l'infection chronique) malgré la « perte » de l'Ac anti-HBs chez 2/3 des adolescents : ce qui compte, c'est la mémoire B, plus que le taux d'anticorps

	Vaccinated
	All
Baseline	382/492 (77.6%)
Anti-HBs ≥10 IU/l	128 (33.5%) (28.8–38.5)
GMC if anti-HBs detected	31.4 (26.0–38.0)

Observational study of vaccine efficacy 14 years after trial of hepatitis B vaccination in Gambian children

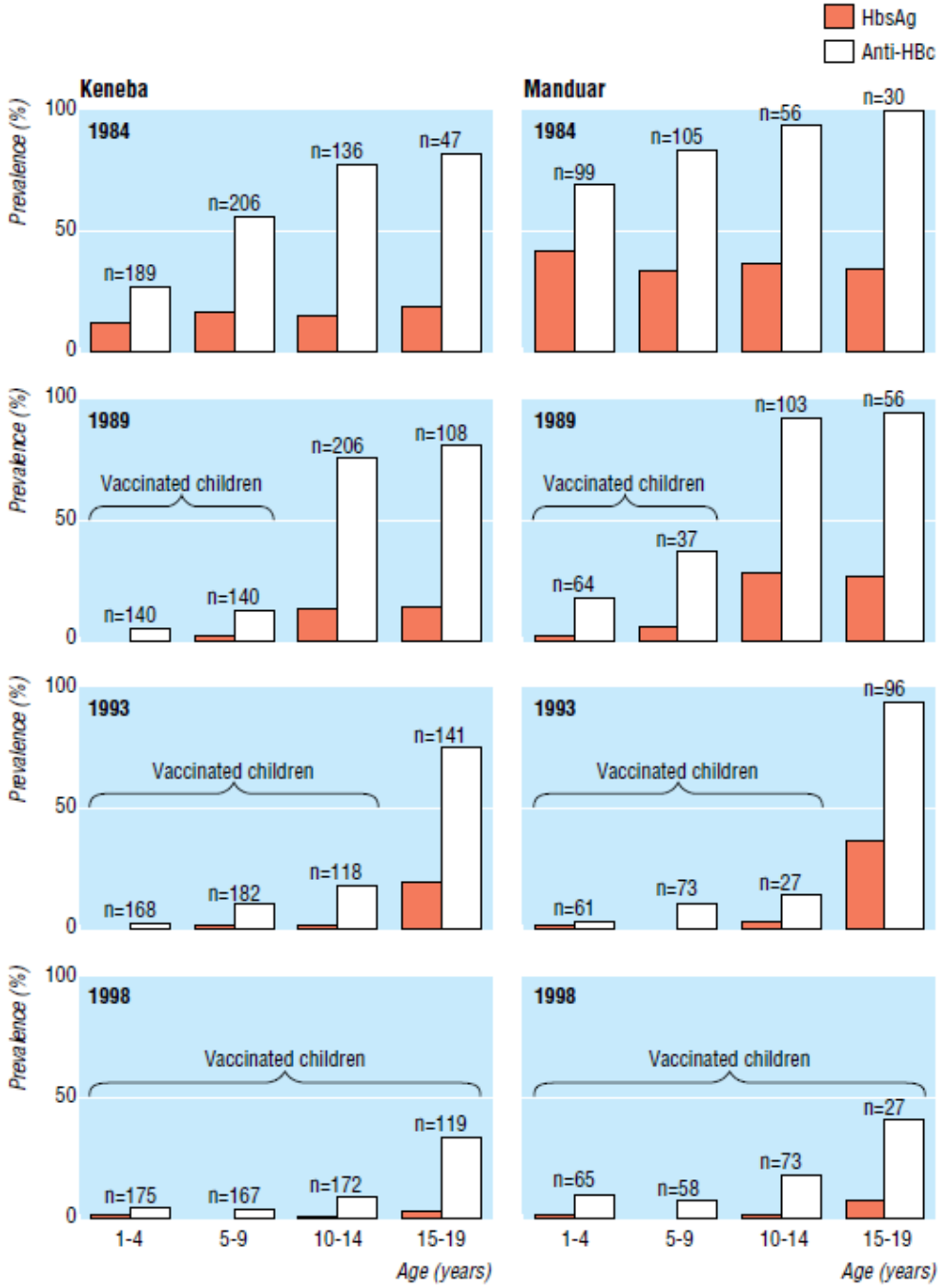
Hilton Whittle, Shabbar Jaffar, Michael Wansbrough, Maimuna Mendy, Uga Dumpis, Andrew Collinson, Andrew Hall

Efficacité vaccinale
malgré la perte de l'Ac anti-HBs
chez 1/3 des adolescents

2002

Table 2 Concentrations of antibody to hepatitis B surface antigen (anti-HbsAg) and number infected over time among vaccinated children in groups 1-3

Year of survey	No tested*	Proportion (%) with anti-HBsAg <10 mIU/ml among those uninfected†	Geometric mean (95% CI) anti-HBsAg (mIU/ml)‡ among those uninfected	No infected at time of survey	No ever infected§
Group 1					
1985	53	8/47 (17)	302 (216 to 422)	7	7
1989	48	9/37 (24)	60 (37 to 97)	10	11
1993	47	4/30 (13)	31 (21 to 46)	15	19
1998	52	11/30 (37)	67 (38 to 120)	21	24
Group 2					
1985	57	3/50 (6)	579 (421 to 796)	7	7
1989	53	10/42 (24)	65 (45 to 95)	11	11
1993	49	5/37 (14)	32 (24 to 44)	10	16
1998	56	12/34 (35)	60 (30 to 120)	18	23
Group 3					
1985	62	0/62 (0)	1045 (758 to 1442)	2	2
1989	61	3/55 (5)	134 (83 to 216)	4	6
1993	59	5/47 (11)	97 (59 to 162)	8	12
1998	63	17/47 (36)	79 (45 to 140)	14	17

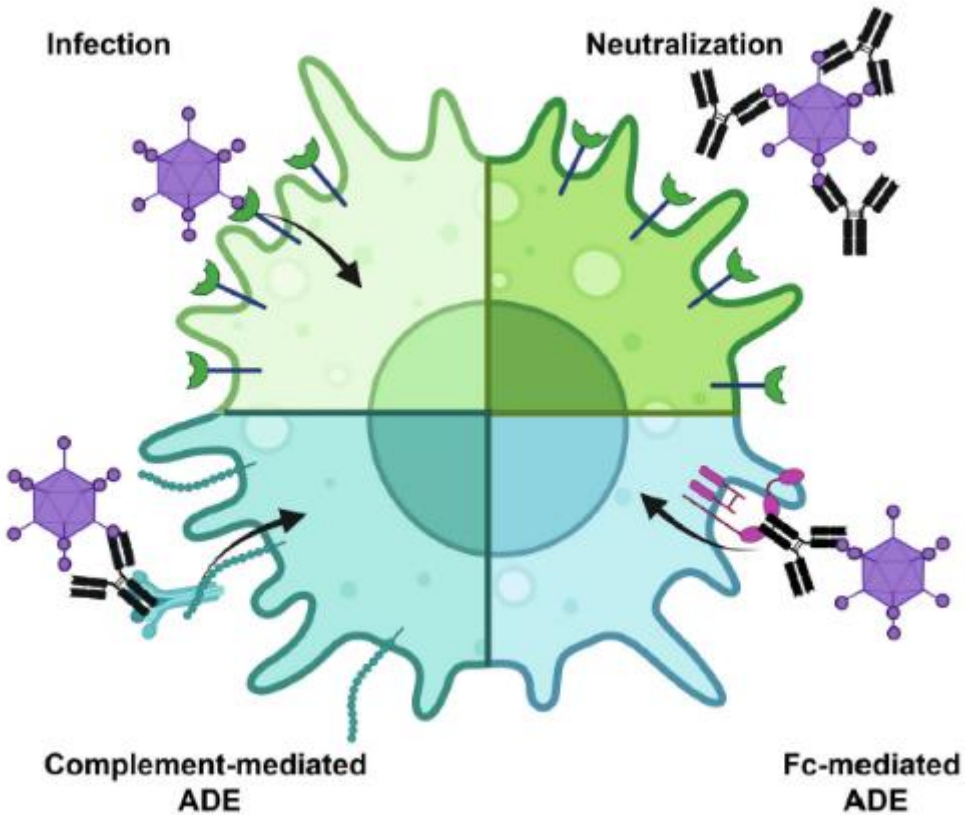


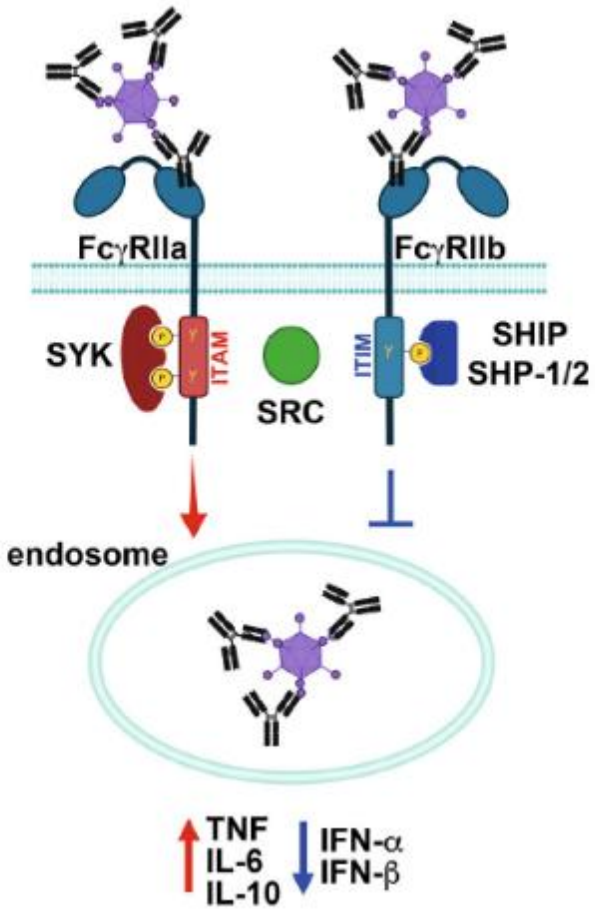
Effect of vaccination against hepatitis B infection on prevalence of hepatitis B virus surface antigen (HBsAg) and hepatitis B virus core antibody (anti-HBc) in two villages in the Gambia

Un corrélat de vulnérabilité ? Les anticorps facilitants

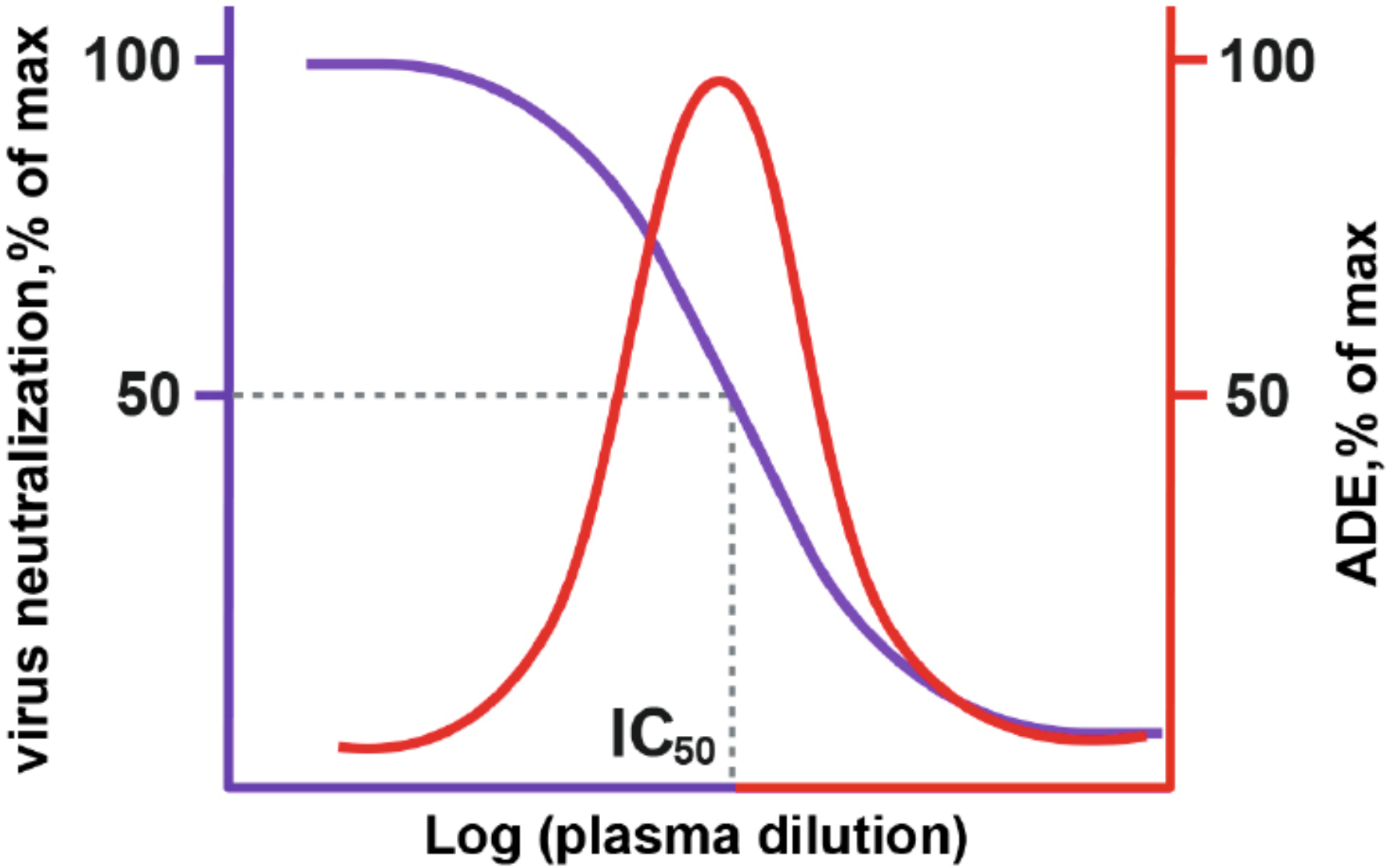
Molecular Mechanisms of Antibody-Dependent Enhancement of Viral Infection

Alexander V. Filatov[1,2,a*], Maria G. Byazrova[1,3], Maria M. Sukhova[1,2], and Alexey G. Prilipov[1,4]





ANTIBODY-DEPENDENT ENHANCEMENT OF INFECTION



En conclusion

- Complexité persistante
- Un énorme champ de recherche
- Une dissection des réponses immunes de plus en plus détaillée ; comment distinguer *surrogate* et *correlate* ?
- Nouvelles données cruciales pour la mise au point de vaccins