



المركز الإستشفائي الجامعي
مفعد السادس
مراكش
Centre Hospitalier Universitaire
Mohammed VI
Marrakech

Vaccination des Enfants et Maladies Neurologiques

Mohammed Bouskraoui
mo.bouskraoui@uca.ma



كلية الطب
والصيدلة - مراكش
FACULTÉ DE MÉDECINE
ET DE PHARMACIE - MARRAKECH

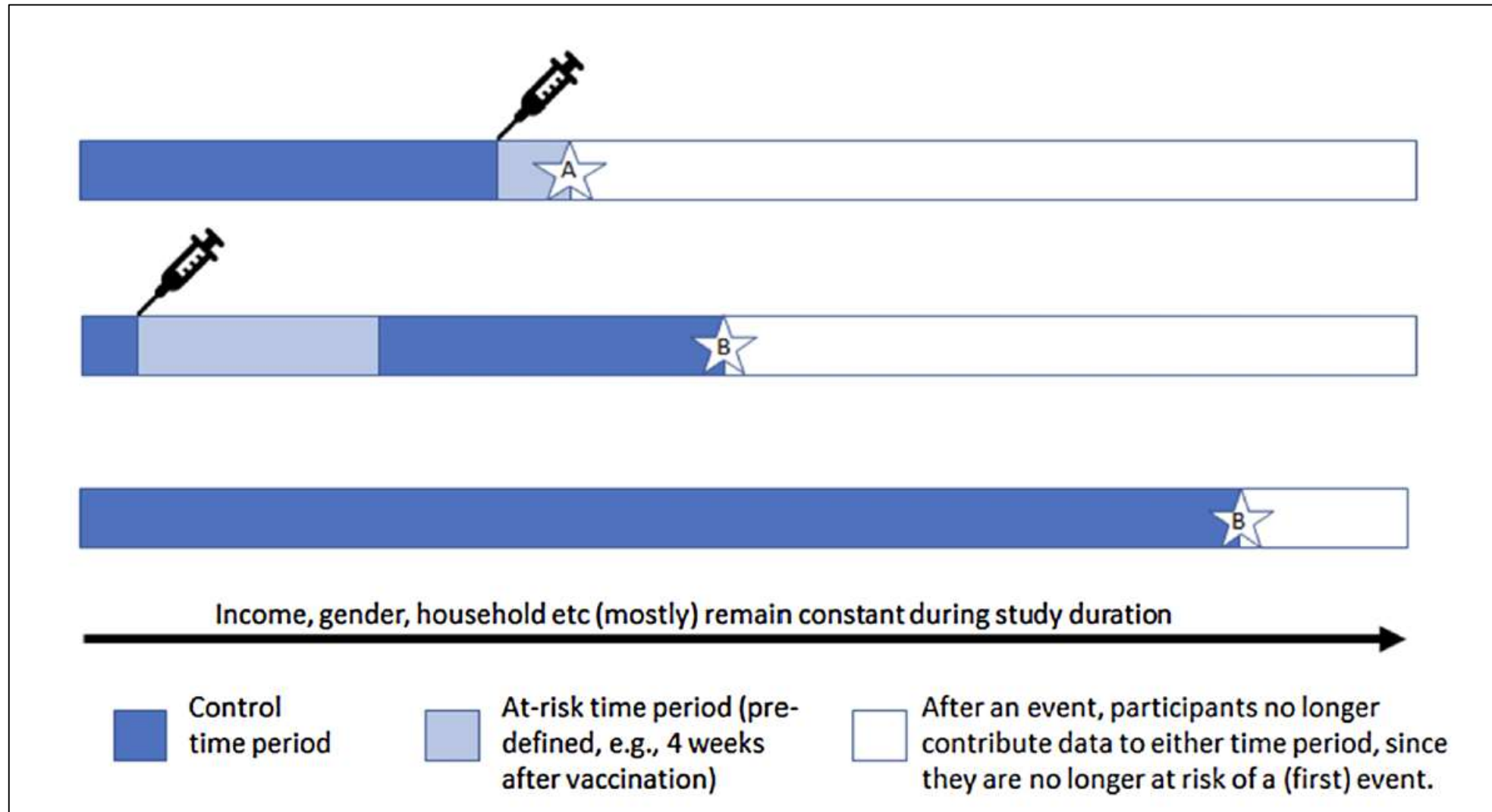
Les vaccinations peuvent-elles aggraver les maladies auto-immunes ?

Maladies dysimmunitaires diagnostiquées chez des jeunes femmes dans la **semaine** suivant l'injection d'un **placebo** à 0-1-6 mois (taux pour 1000 000)

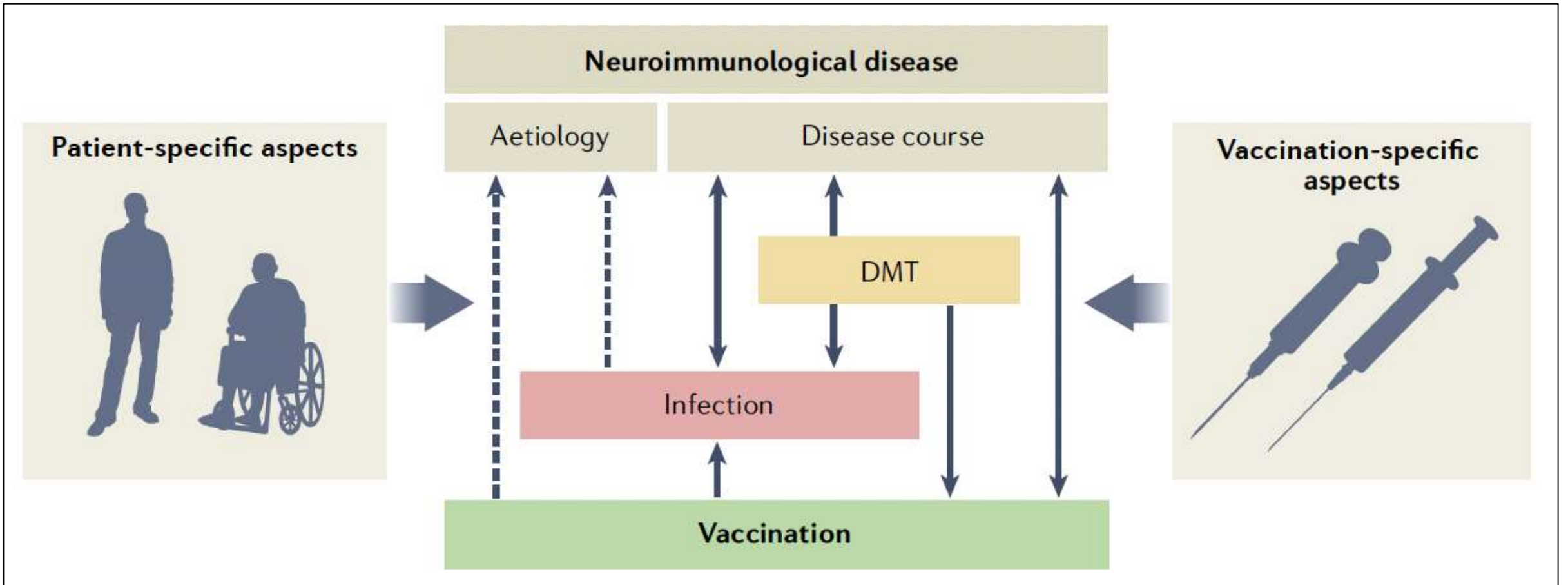
Maladies	Adolescentes	Adultes
Asthme	188	212
Allergie	106	174
Diabète	29	39
Thyroïdite	9	166
Mies infl. Digestives	10	20
LEAD	5	18
SEP ou NO	2	7



Interprétation des événements indésirables neurologiques associés au vaccin



La vaccination des maladies neurologiques

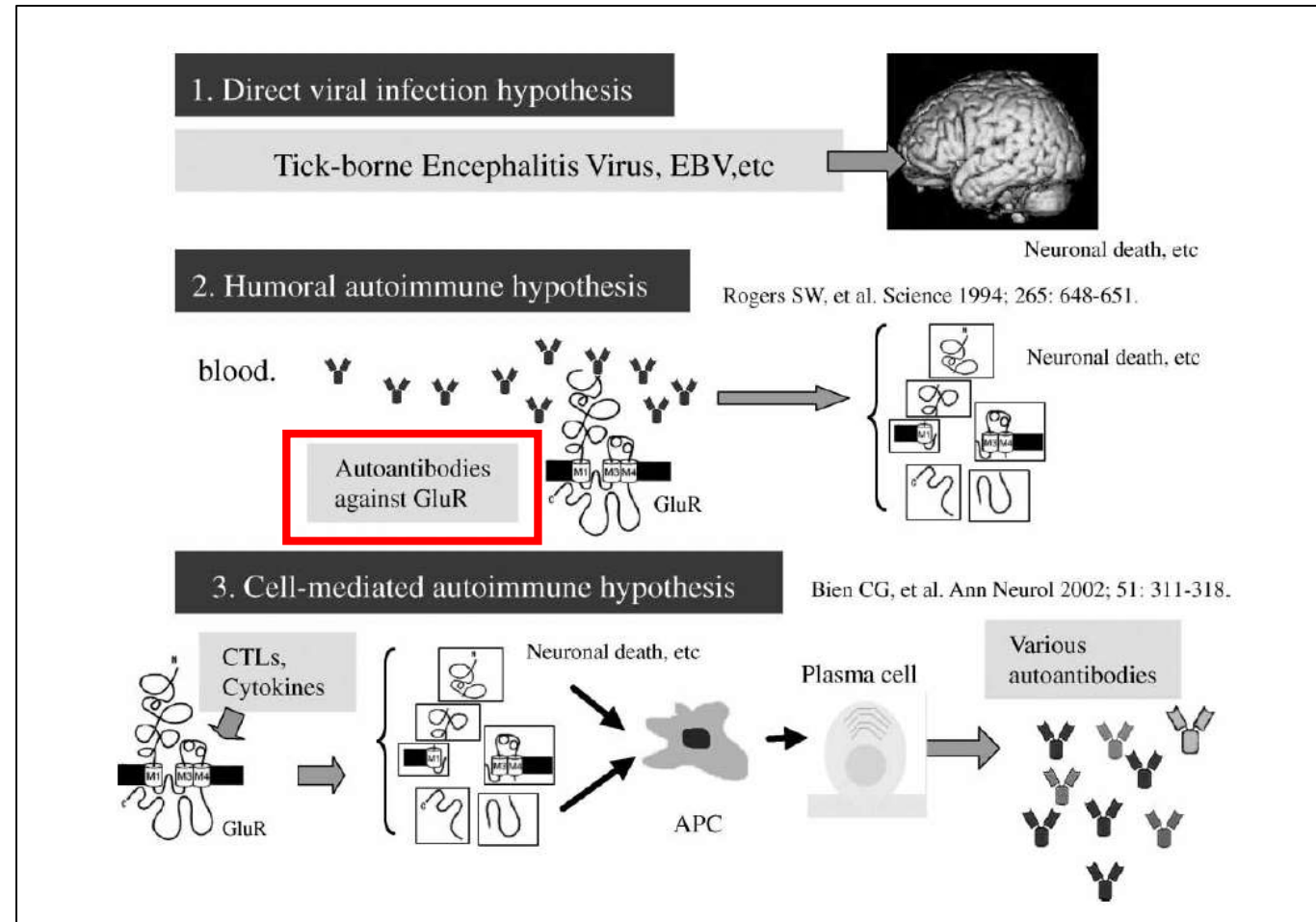
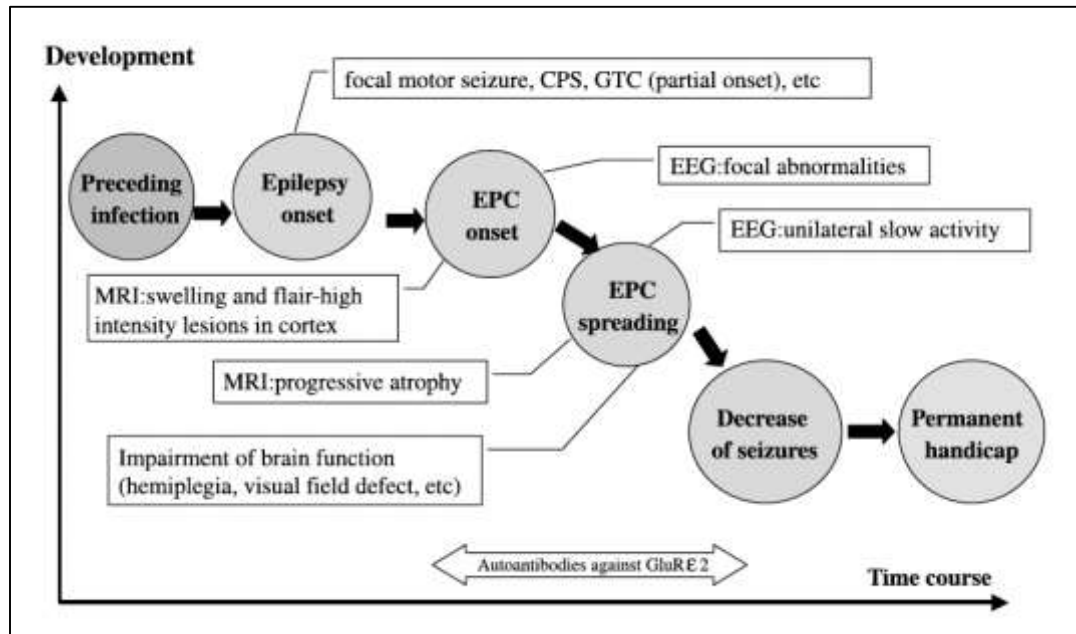


Vaccination des enfants avec maladies neuro-musculaires d'origine inflammatoire

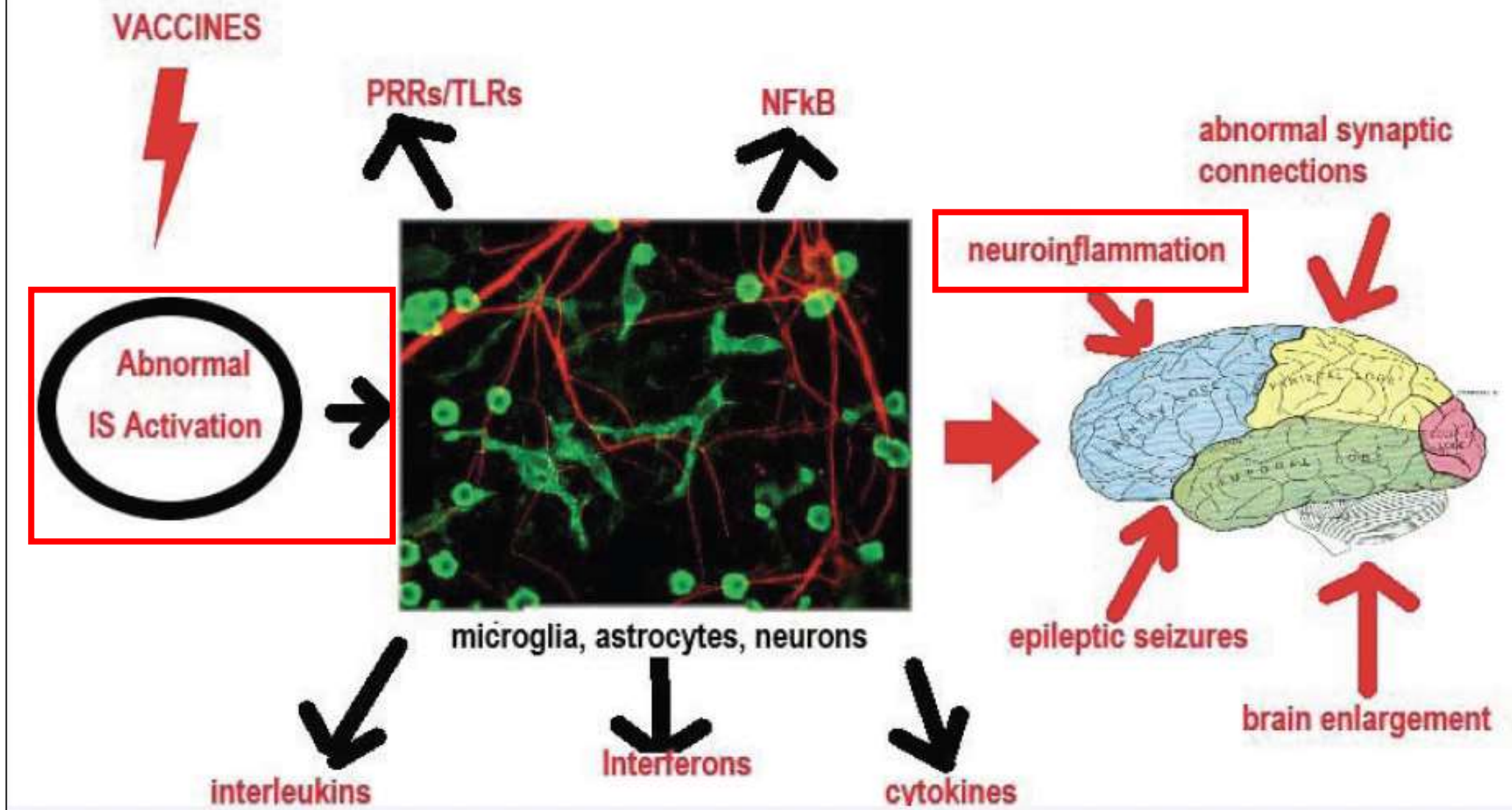
Vaccine	Type	Safety in acquired NMD
Influenza	Inactivated	Considered safe
Hepatitis B	Inactivated	Considered safe
HPV (Human Papillomavirus)	Inactivated	Probably safe
Tetanus	Inactivated	Considered safe
Meningococcal (MCV4)		Considered safe
Rabies	Inactivated	Probably safe
Polio vaccine	inactivated	Probably safe
Varicella	Live attenuated	Probably safe*
Yellow fever	Live attenuated	Probably safe*
BCG (Bacillus Calmette-Guerin)	Live attenuated	Probably safe*
MMR (Morbilli-rubela-mumps)	Live attenuated	Probably safe*

Legend: *Contraindicated in patients on immunosuppressive treatment. Should be administered prior onset of immunosuppressive treatment.

Syndrome de Rasmussen : Mimétisme moléculaire et classe HLA I



Vaccine Associated Regressive Autism (VARA)



*Peut-t-on faire un
Pentavalent à Hassan qui
présente une sclérose
tubéreuse de Bourneville
révélée par des
convulsions à l'âge
de 1 mois?*

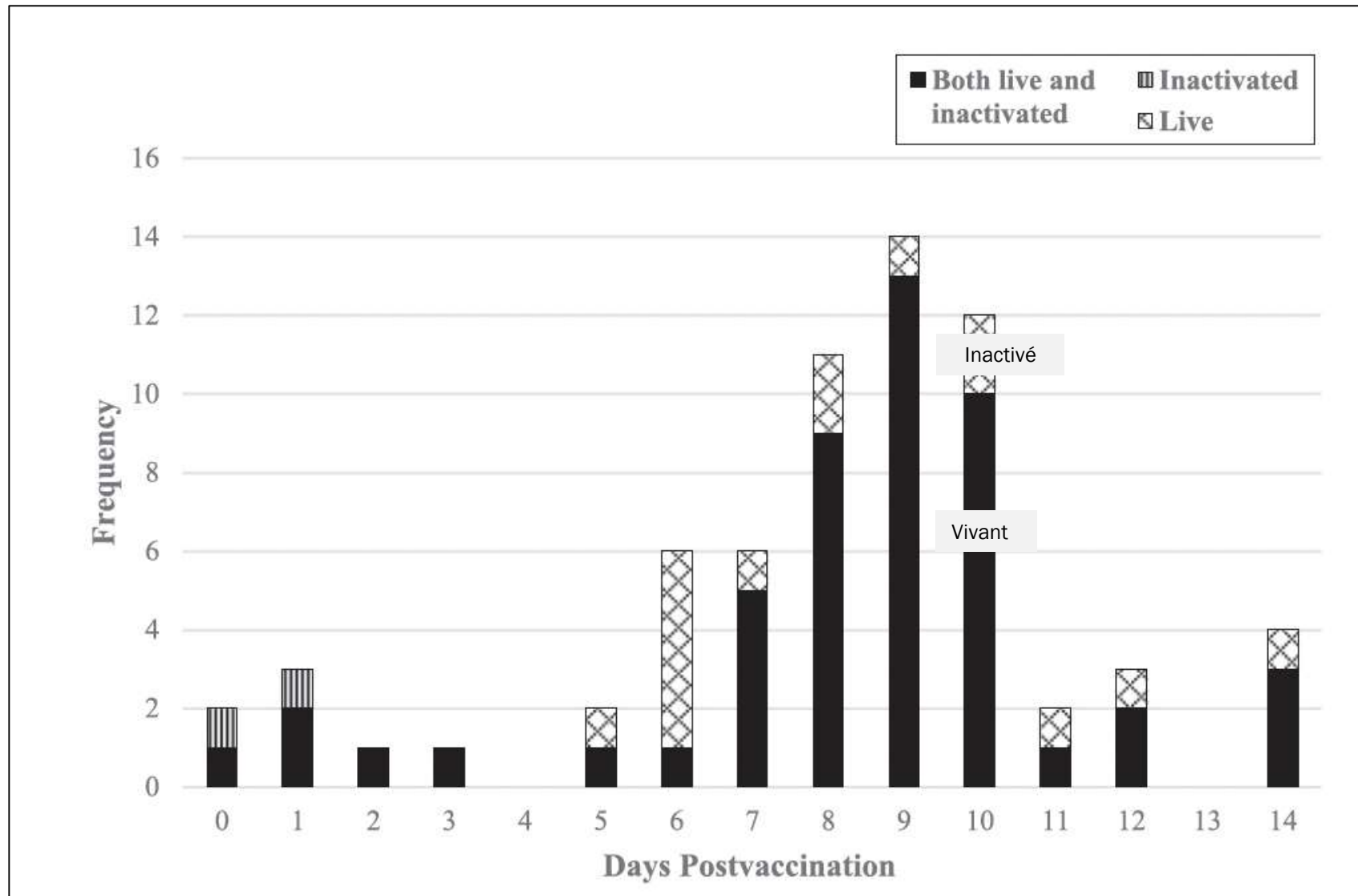


Convulsions suite à la vaccination

Vaccine type	Vaccines	Risk interval (days after vaccination)	Febrile seizure risk
Live-attenuated	MMR	5-14	One febrile seizure per 1,150-3,000 vaccinations ^{9,10}
	MMRV	5-14	One additional febrile seizure per 2,600 MMRV vaccinations when compared with MMR+V ^{6,11} No increased risk if administered as dose two ¹²
Inactivated	DTPa	0-2	No increased risk ^{4,13,14}
	TIV	0-2	One febrile seizure per 70,000 vaccinations (2003-04) ¹⁶ One febrile seizure per 300 vaccinations (2010) ¹⁵ No increased risk with current formulation ¹⁸
	TIV + PCV13	0-2	Fivefold increased risk of febrile seizure compared to having the vaccines separately ¹⁷

DTPa, diphtheria/tetanus/acellular pertussis vaccine; MMR, measles/mumps/rubella vaccine; MMR+V, MMR vaccine given concomitantly with varicella zoster virus vaccine; MMRV, measles/mumps/rubella/varicella vaccine; PCV13, 13-valent conjugate pneumococcal vaccine; TIV, trivalent influenza vaccine

Convulsions fébriles après la vaccination

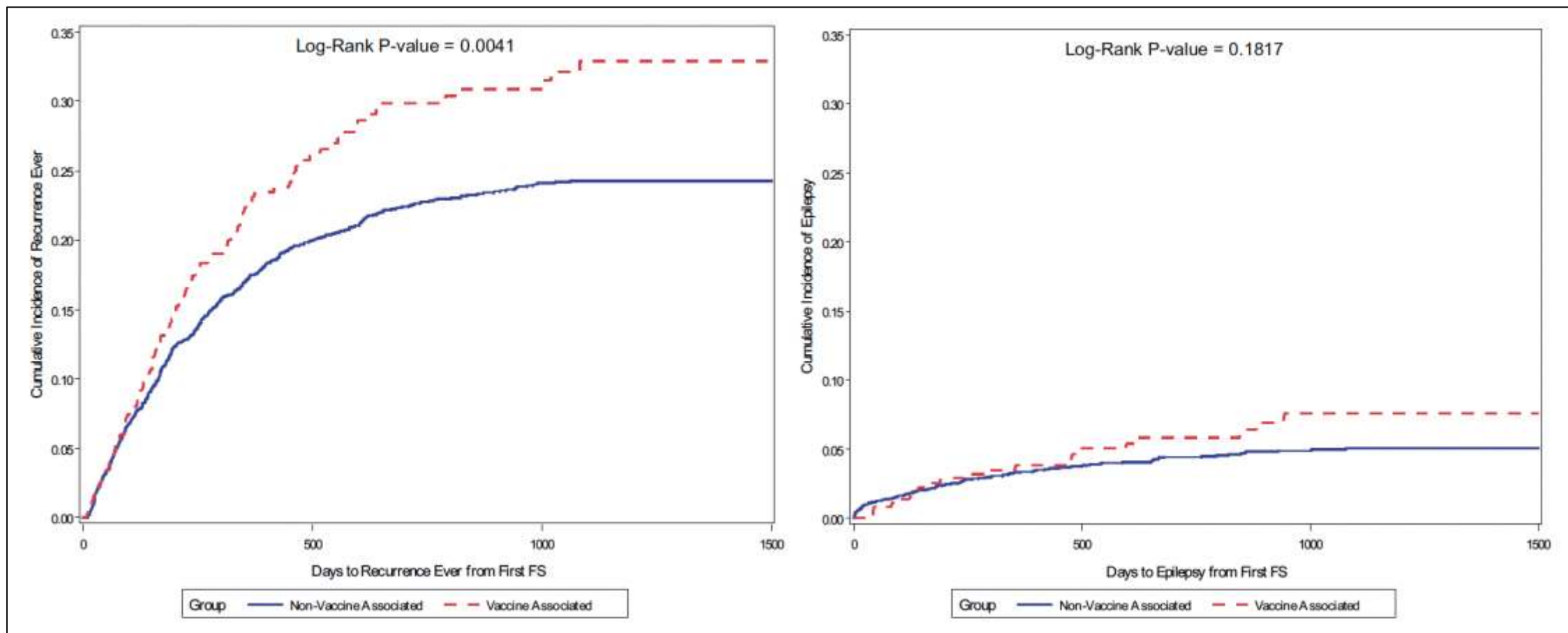


Risque de convulsions fébriles après la vaccination chez les enfants de 6 à 23 mois



Admission en hospitalisation pour convulsions fébriles

Comparaison des enfants atteints de convulsions fébriles associées au vaccin et non associées au vaccin



Vaccination et épilepsies infantiles

Vaccine	Type	Recommendation	Risk interval (Days after vaccination)	FS risk
DTwP [39–42,58]	Inactivated	All children; replace with DTaP in case of personal/family history of FS, epilepsy, DS	0–2	1.5 to 5 times increased risk comparing to non-vaccinated [39–42]
DTaP [42,43]	Subunit (purified antigen)	All children	0–2	No increased risk [42,43,58]
DTaP-IPV-Hib [58]	Inactivated	All children.		No increased risk [58]
*IPV [58]	Inactivated	All children, adolescents		No increased risk [58]
*HepB [58]	Subunit (purified antigen)	All children, adolescents		No increased risk [58]
PCV13 [57]	Subunit (purified antigen)	All children younger than 2 years (PCV13) *	0–3	PCV7 - increased risk alone or combined with TIV or DTaP-IPV-Hib [54,55,58]
PCV7 [54,55,58]				PCV13 - slightly increases risk if combined with TIV [57]
MMR [45–51]	Live attenuated	All children	5-14 (Peak 7–10)	No or slight increased risk if vaccinated age 12–15 months [49–51] Increased risk if delayed vaccination [51]
MMRV [45,50,52,58]	Live attenuated	All children	5-14 (Peak 7–10)	Increased risk comparing to MMR and V administered separately [45,50,52]
Varicella [36,37]	Live attenuated	Patients without exposure, given in two doses	0–2	Increased risk if combined with MMR [45,50,52]
TIV [53–56,59,60]	Inactivated	All individuals 6 months and older	0–2	No increased risk; Increased risk if TIV given in the same day as either DTaP [54], PCV7 [56], or PCV13 [26] vaccines

Événements indésirables suivant la vaccination parmi les enfants atteints d'épilepsie (Canada)

Risk Window	Inactivated Immunizations			Live immunizations		
	Children With Epilepsy aRI*	Children Without Epilepsy aRI*	Adjusted RIR	Children With Epilepsy aRI	Children Without Epilepsy aRI	Adjusted RIR
0–7 days	0.9 (0.8–1.0)	0.9 (0.9–1.0)	1.0 (0.9–1.1)	0.9 (0.8–1.0)	0.9 (0.9–0.9)	1.0 (0.8–1.1)
8–14 days	1.1 (1.0–1.2)	1.1 (1.1–1.1)	1.0 (0.9–1.1)	1.1 (1.0–1.3)	1.2 (1.1–1.2)	1.0 (0.8–1.1)
15–21 days	0.9 (0.9–1.0)	1.0 (1.0–1.0)	1.0 (0.9–1.1)	1.0 (0.9–1.1)	1.0 (1.0–1.0)	1.0 (0.9–1.1)
22–28 days	1.0 (0.9–1.1)	1.0 (1.0–1.0)	1.0 (0.9–1.1)	1.0 (0.8–1.1)	1.0 (1.0–1.0)	0.9 (0.8–1.1)
0–28 days	1.0 (0.9–1.1)	1.0 (1.0–1.0)	1.0 (1.0–1.1)	1.0 (0.9–1.1)	1.0 (1.0–1.0)	1.0 (0.9–1.0)
0–2 days	0.9 (0.8–1.0)	0.8 (0.8–0.8)	1.2 (1.0–1.4)	—	—	—
7–10 days	—	—	—	1.3 (1.1–1.5)	1.3 (1.2–1.3)	1.0 (0.9–1.2)

Bold-faced font indicates 95% CI does not include the null.

*Adjusted for season and age.

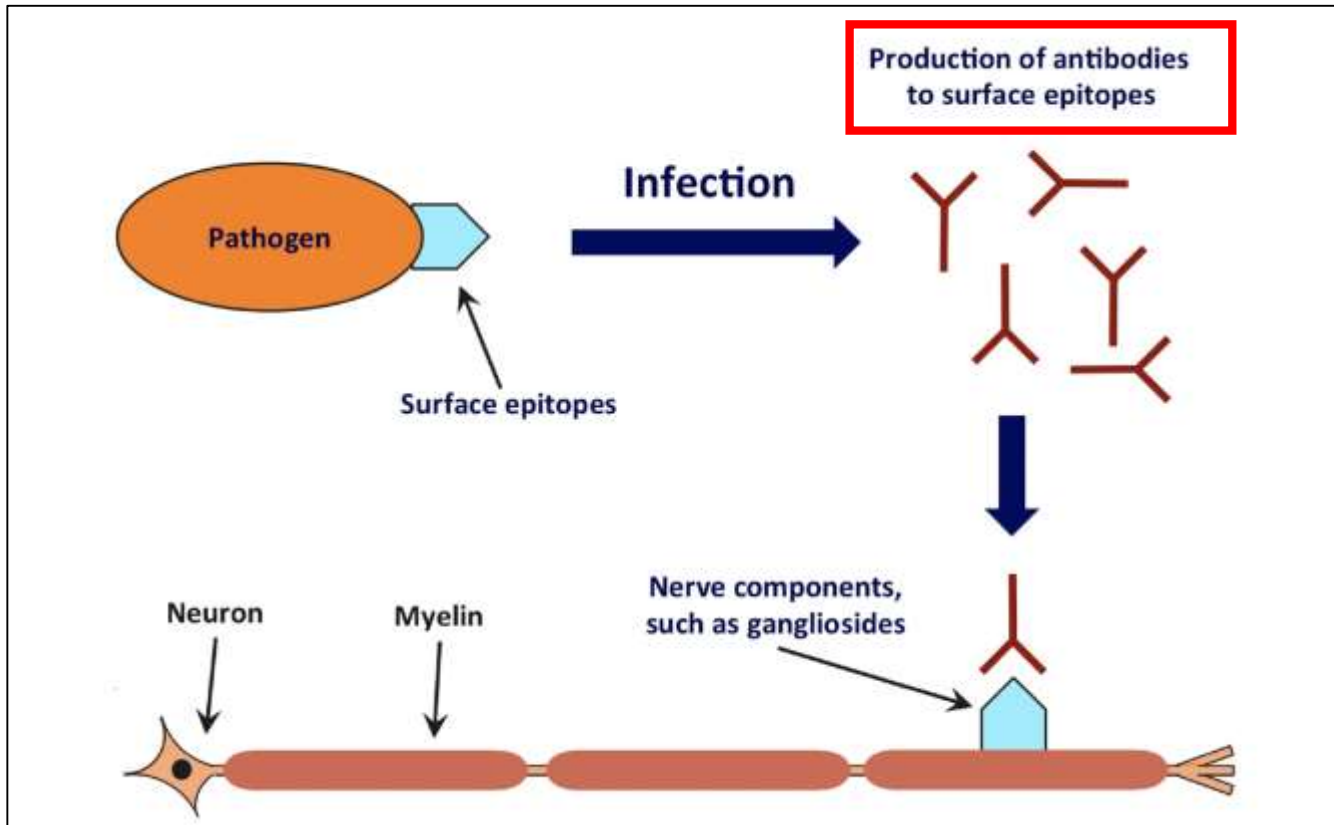
^aRI indicates adjusted relative incidence; CI, confidence interval; ED, Emergency Department; RIR, relative incidence ratio.

Pediatr Infect Dis J 2020;39:454–459

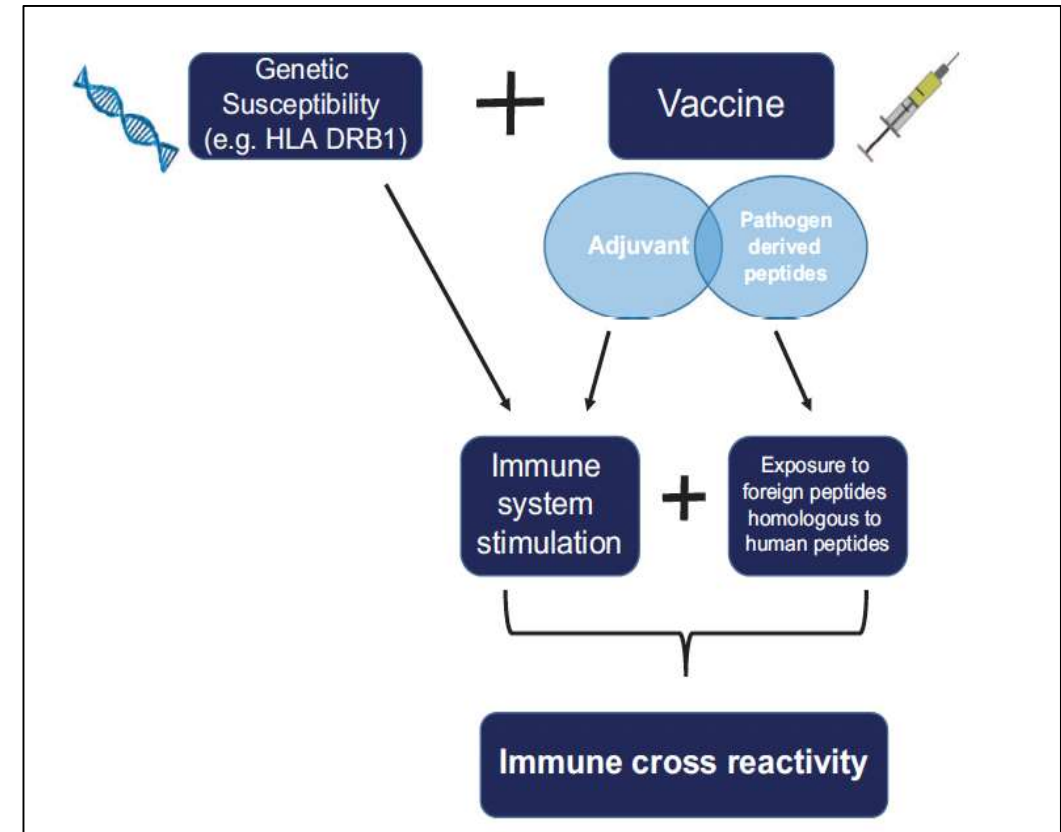
Gravité des infections : rougeole, coqueluche, méningite....

Infection émergente, vaccination et Syndrome du Guillain-Barré

Auto-immunité induite par les vaccins : Mimétisme et réaction immunitaire croisée



Neurol Ther (2021) 10:523–537

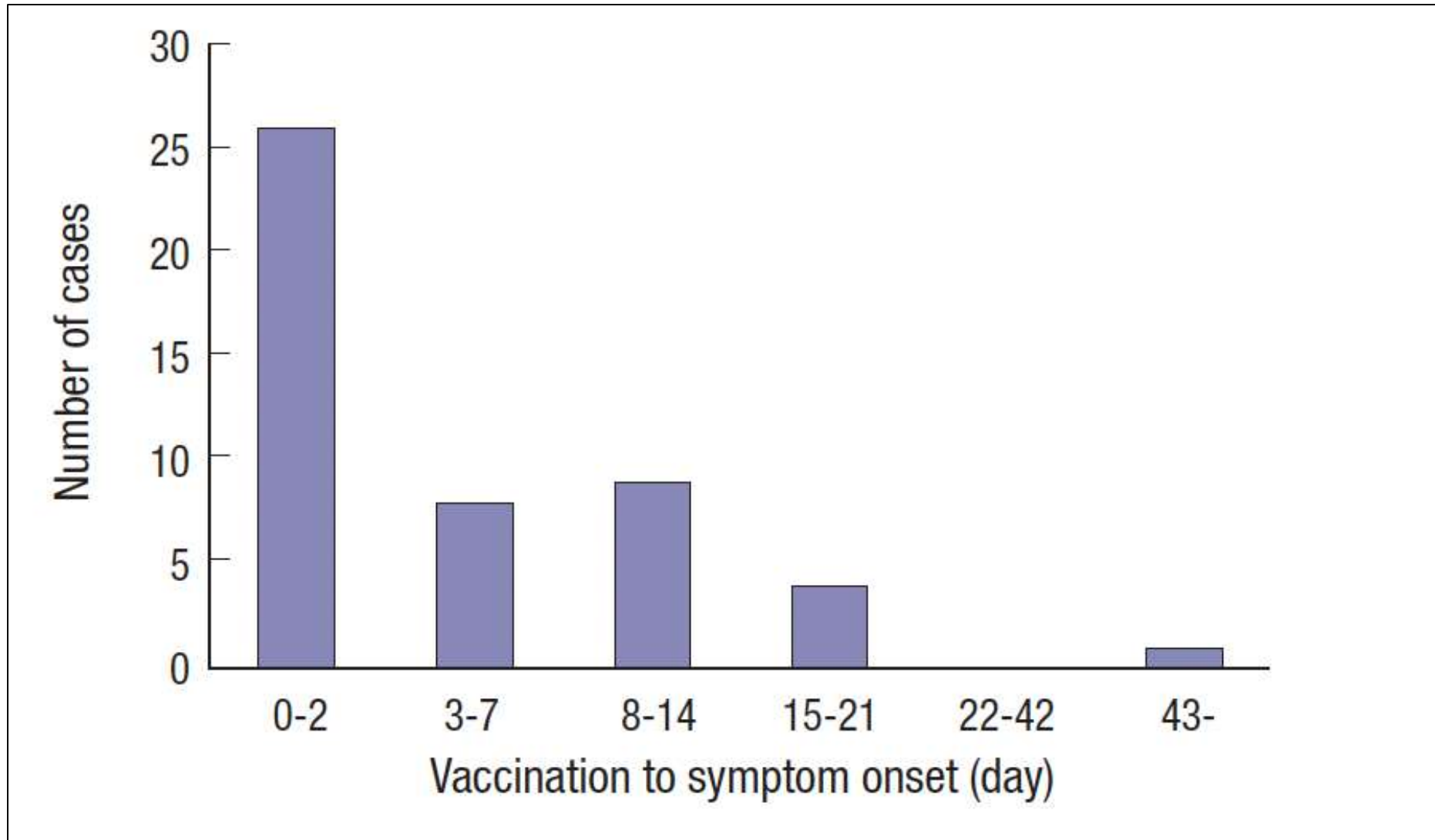


Cellular & Molecular Immunology (2018) 14, 1–9

Les vaccins et le risque du syndrome de Guillain-Barré

	Age ≤ 18 years		OR (95% CI)	Adjusted OR (95% CI)	Age > 18 years		OR (95% CI)	Adjusted OR (95% CI)
	No. (%) of vaccinated	No. (%) of nonvaccinated			No. (%) of vaccinated	No. (%) of nonvaccinated		
Recurrence	1 (33.33)	2 (66.67)	0.83 (0.07–9.50)	0.85	8 (21.62)	29 (78.38)	1.23 (0.55–2.73)	1.18
Recurrence-free	39 (37.50)	65 (62.50)		(0.12–8.68)	201 (18.32)	896 (81.68)		(0.49–2.65)
Total	40 (37.38)	67 (62.62)			209 (18.43)	925 (81.57)		

Caractéristiques cliniques du syndrome de Guillain-Barré post-vaccination en Corée



Syndrome de Guillain-Barré potentiellement attribuables à une vaccination

Hôpital Raymond-Poincaré (Garches) :1996 - 2006



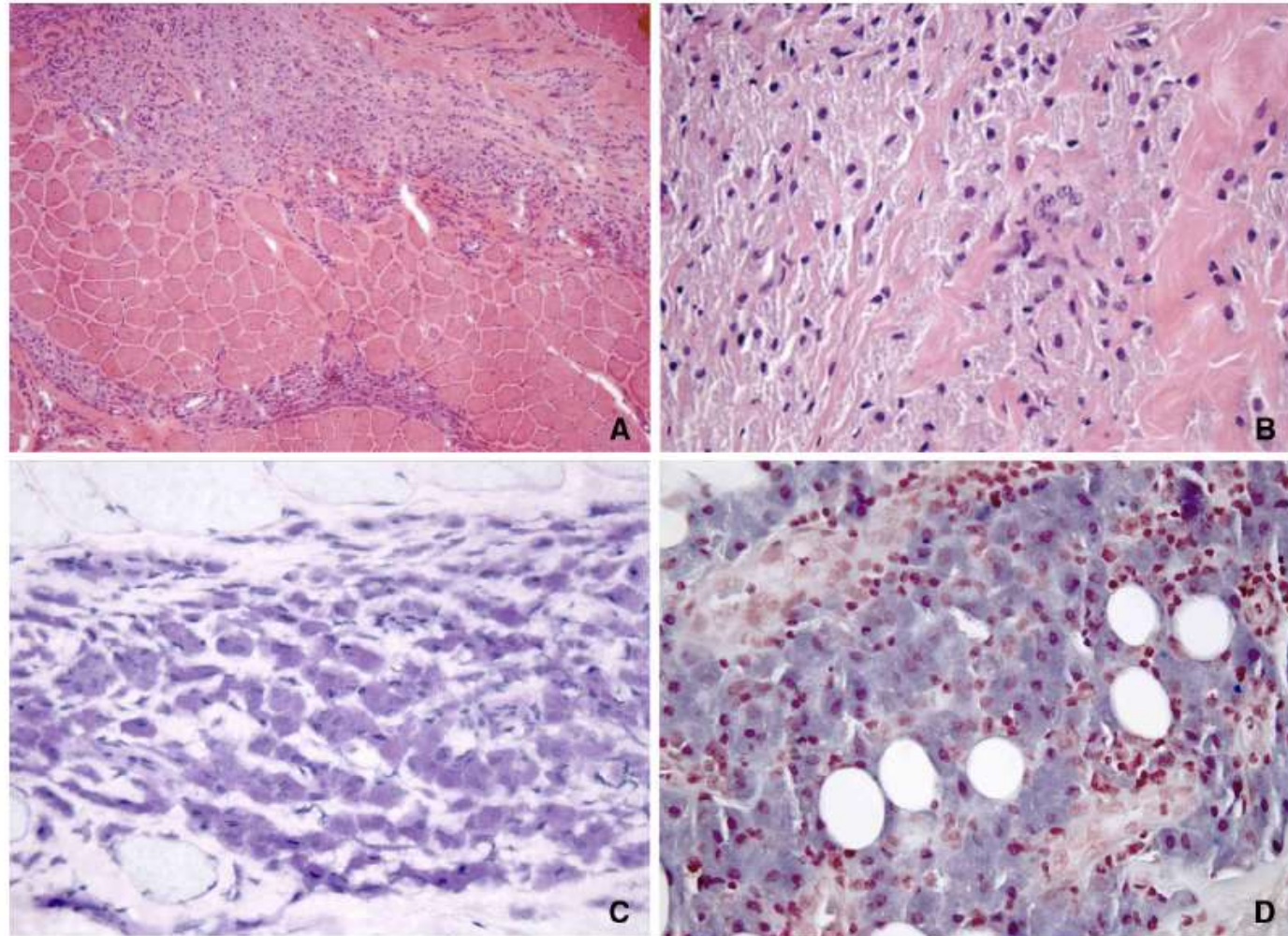
	Nombre de sujets vaccinés*	Nombre de sujets vaccinés sans autre étiologie**	Nombre de sujets vaccinés sans autre étiologie et sans prodromes***
Tous vaccins	16 (3,2 %)	10 (2,0 %)	7 (1,4 %)
Vaccin contre la grippe	7 (1,4 %)	4 (0,8 %)	2 (0,4 %)
Autre vaccin	9 (1,8 %)	6 (1,2 %)	5 (1,0 %)

* Au cours des 6 semaines ayant précédé le SGB.

** Parmi les 4 étiologies systématiquement recherchées : *C. jejuni*, CMV, EBV et *M. pneumoniae*.

*** Patients n'ayant présenté aucun syndrome grippal, ni signe d'infection respiratoire ou digestive au cours des 6 semaines ayant précédé le SGB.

Myo-fasciite à macrophages et vaccination : Conséquence ou coïncidence ?



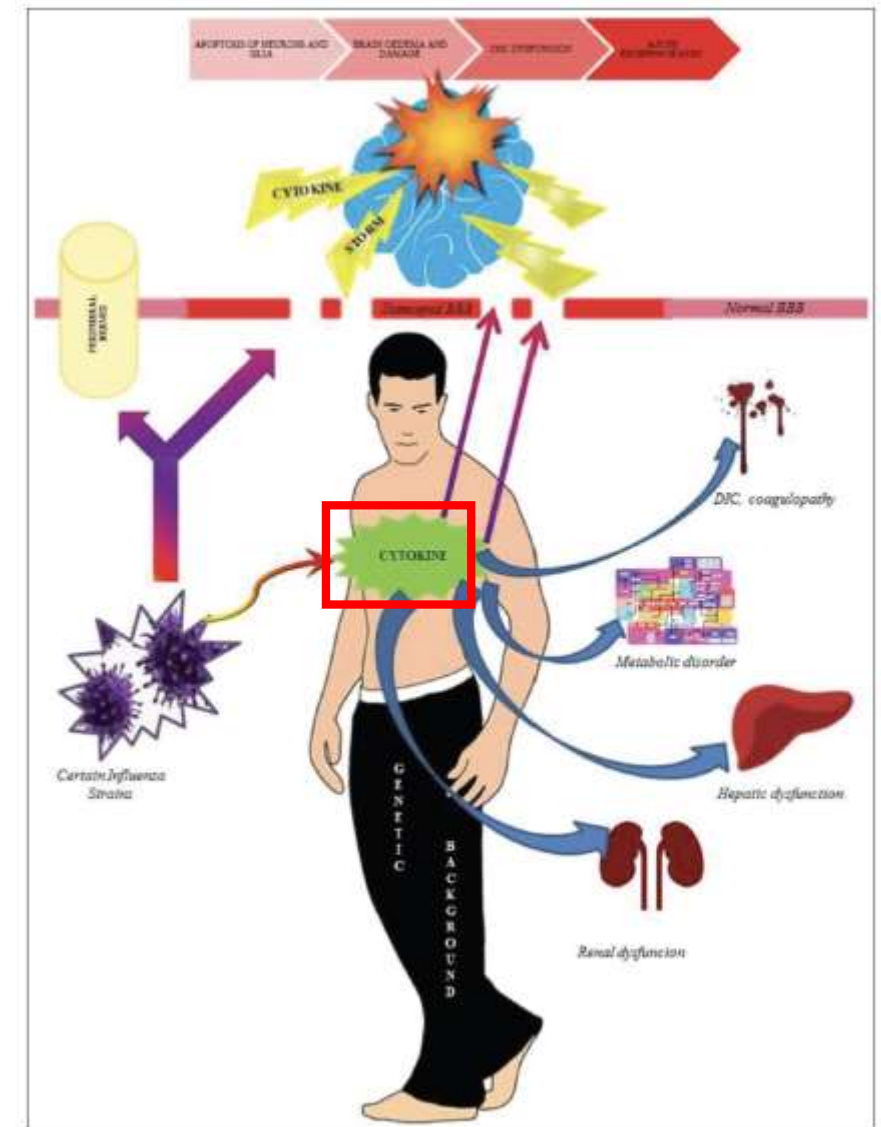
Complications neuro-musculaires post-grippales

Complications neurologiques chez les enfants hospitalisés pour des infections grippales

Seizures	23 (79.3%)
Febrile	21
Afebrile	2
Tonic-clonic	19
Atonic	4
<5 minutes	12
5–10 minutes	6
>10 minutes	5
Encephalopathy	2 (6.9%)
Others	3 (13.8%)
Total (%)	29 (100)

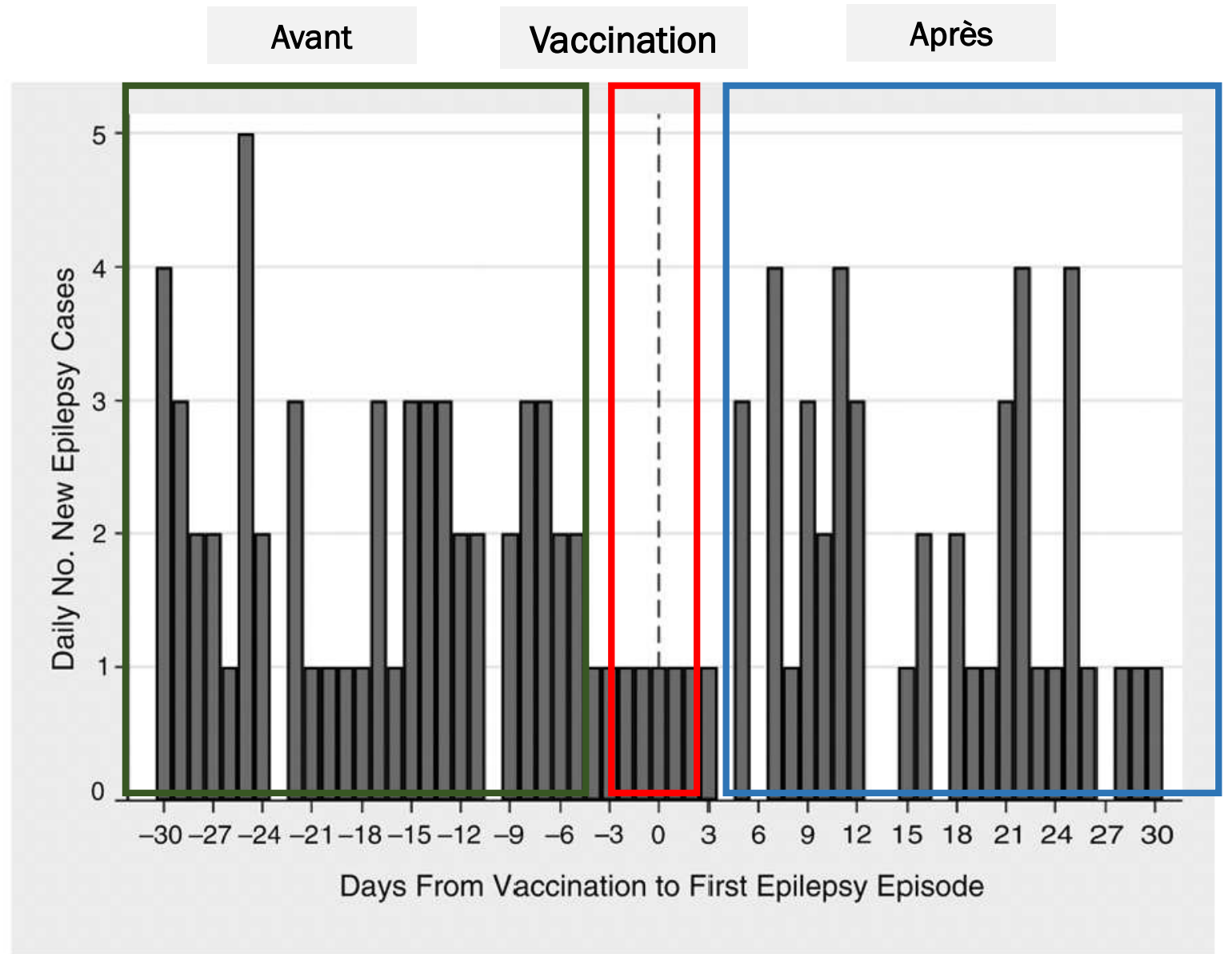
Pediatr Infect Dis J 2020;39:789–793)

- Grippe Maladie :
- Vaccination :



L'épilepsie chez les enfants après la vaccination contre la grippe pandémique

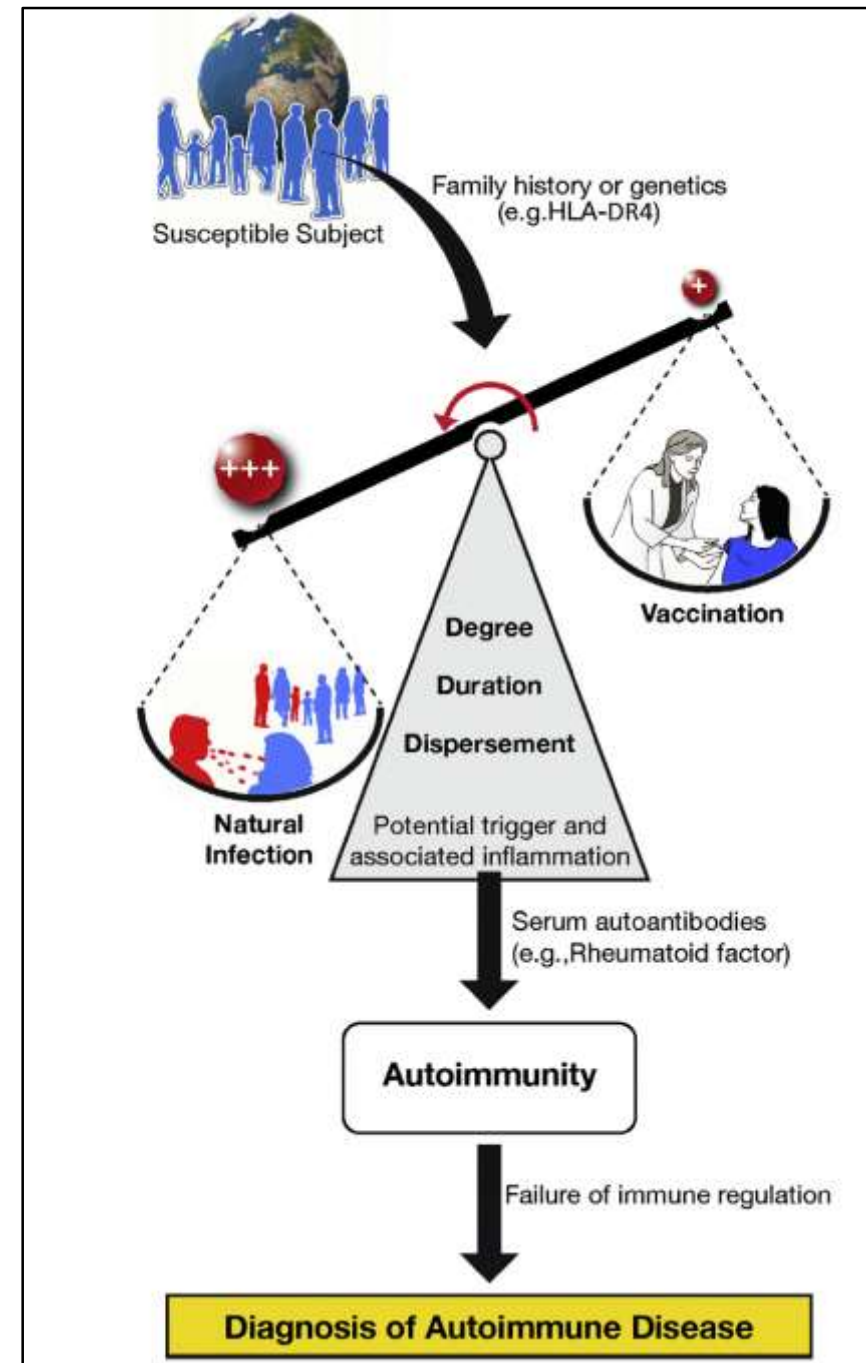
Pediatrics. 2018;141(3):e20170752



Narcolepsie, grippe pandémique A(H1N1) de 2009 et vaccination pandémique contre la grippe

Journal of Autoimmunity 50 (2014) 1e11

Autoimmune disease	Infection
Multiple sclerosis	Herpes virus type 6 [113,114]
Guillain-Barré syndrome	<i>Campylobacter jejuni</i> [115]
	<i>Mycoplasma pneumoniae</i> [116]
Type 1 diabetes	Cytomegalovirus [117,118]
Lyme arthritis	<i>Borrelia burgdorferi</i> [119,120]
Chagas disease/myocarditis	<i>Trypanosoma cruzi</i> [121,122]



Syndrome du Guillain-Barré et vaccins anti-grippaux : Preuves actuelles

Authors/Year	Study location	Design	Influenza vaccine	Risk
Salmon et al. 2013	USA	Meta-analysis	A (H1N1) 2009	IRR=2.35 (95% CI 1.2-4.01)
Dodd et al. 2013	International*	Meta-analysis	A (H1N1) 2009	RI= 2.09 (95%CI 1.28-3.42)
Martín Arias et al. 2015	International	Meta-analysis	A(H1N1) 2009	RR= 1.84 (95%CI 1.36-2.50)
			Seasonal	RR= 1.22 (95%CI 1.01-1.48)

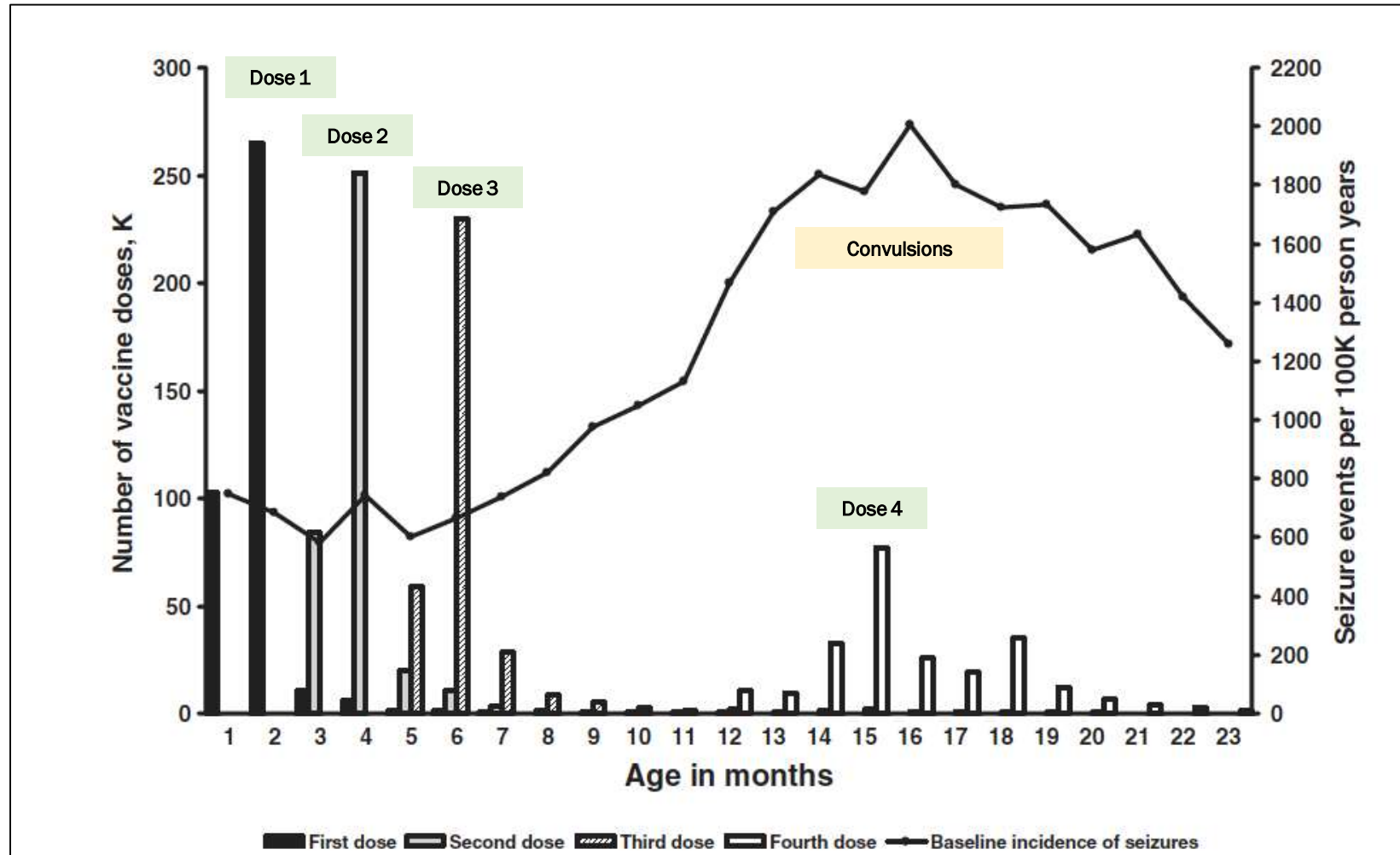
*Australia, Canada, China, Denmark, Finland, The Netherlands, Singapore, Spain, The United Kingdom and The United States Databases.

Encéphalopathie après la vaccination anti-coqueluche entier ou après la vaccination anti-rougeole

Etiology	DTP			MMR		
	Exposed n (row %)	Unexposed n (row %)	Total n (col %)	Exposed n (row %)	Unexposed n (row %)	Total n (col %)
Known	15 (7)	205 (93)	220 (49)	1 (0)	219 (100)	
Suspected/unconfirmed*	15 (17)	71 (83)	86 (19)	4 (5)	82 (95)	
Unknown	19 (13)	127 (87)	146 (32)	3 (2)	143 (98)	146 (32)
All	49 (11)	403 (89)	452 (100)	8 (2)	444 (98)	452 (100)

*Includes cases in which a diagnosis such as viral meningitis was unconfirmed by a specific laboratory test.

Absence d'association entre le vaccin anti-coquelucheux acellulaire et les convulsions dans la petite enfance



Comparaison des vaccins anti-coquelucheux à germes entiers et anti-coquelucheux acellulaires

Type of reaction	Incidence per million whole-cell pertussis vaccines	Incidence per million acellular pertussis vaccines	Odds ratio	Attributable odds ratio percent association	Statistical significance	95% Odds ratio confidence interval
Emergency department visits	72	32	2.3	56	$P < 0.0001$	2.10–2.4
Life-threatening reactions	2.5	1.0	2.5	60	$P = 0.0001$	1.60–4.0
Hospitalizations	16	6.2	2.6	60	$P < 0.0001$	2.10–3.1
Disabilities	1.4	0.38	3.6	72	$P = 0.0002$	1.80–7.1
Deaths	2.7	1.5	1.8	44	$P = 0.009$	1.20–2.8
Seizures	13.4	3.6	3.7	73	$P < 0.0001$	3.00–4.6
Infantile spasms	0.39	0.11	3.4	71	$P = 0.04^*$	–
Encephalitis/ encephalopathy	0.78	0.095	8.2	88	$P < 0.0001$	2.70–25
Autism	0.49	0.11	4.4	77	$P = 0.03$	1.30–14
Sudden infant death syndrome (SIDS)	1.5	0.87	1.7	41	$P = 0.03^*$	–
Speech disorders	0.78	0.23	3.4	70	$P = 0.01$	1.40–8.3
Cerebellar ataxia	0.29	0.27	1.1	9	$P = 0.85$	0.31–3.8

P value determined using Fisher's exact test statistic.

Incidence des épisodes d'hypotonie-hypo-réactivité associés au vaccin combiné DTC/Hib Programme national de vaccination (Brésil)

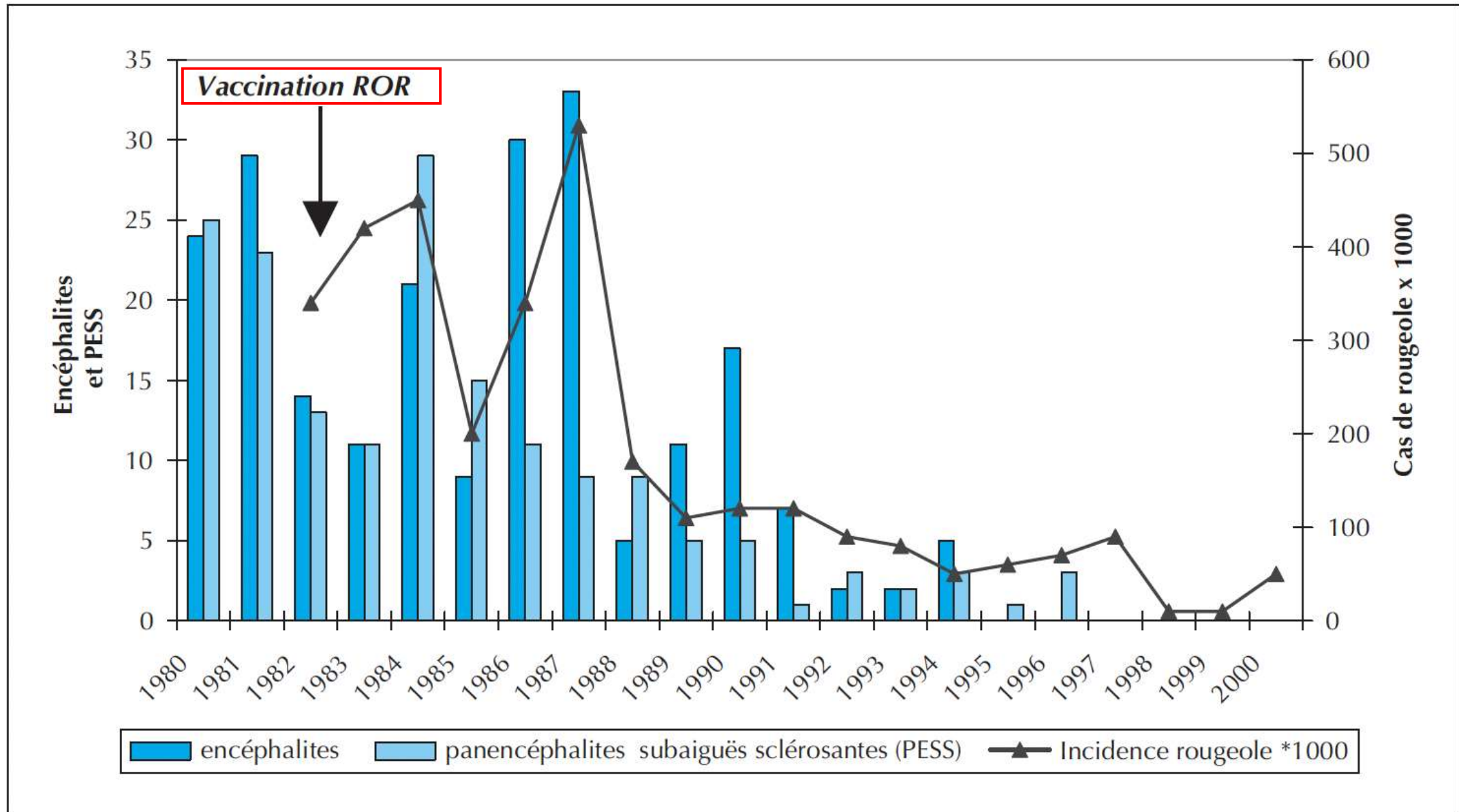
Author, year	Doses per child	Doses of DTwP	HHE	Convulsions
Stehr, 1998 ¹²	4	16,424	1/16,667	1/5,556
Stehr, 1998 ¹²	3	11,962	1/11,962	1/5,981
Greco, 1996 ¹³	3	13,520	1/1,492	1/4,545
Gustafsson, 1996 ¹⁴	3	6,143	1/1,234	1/6,250
Olin, 1997 ¹⁵	3	60,792	1/1,786	1/4,762
Simondon, 1997 ¹⁶	3	6,595	0	1/2,564
Cody, 1981 ¹	5	15,752	1/1,750	1/1,750
Cody, 1981 ¹	3	12,685	1/1,409	1/2,114
Vigat, 2004*	1 [†]	20,925	1/1,495	1/5,231

HHE = hypotonic-hyporesponsive episodes.

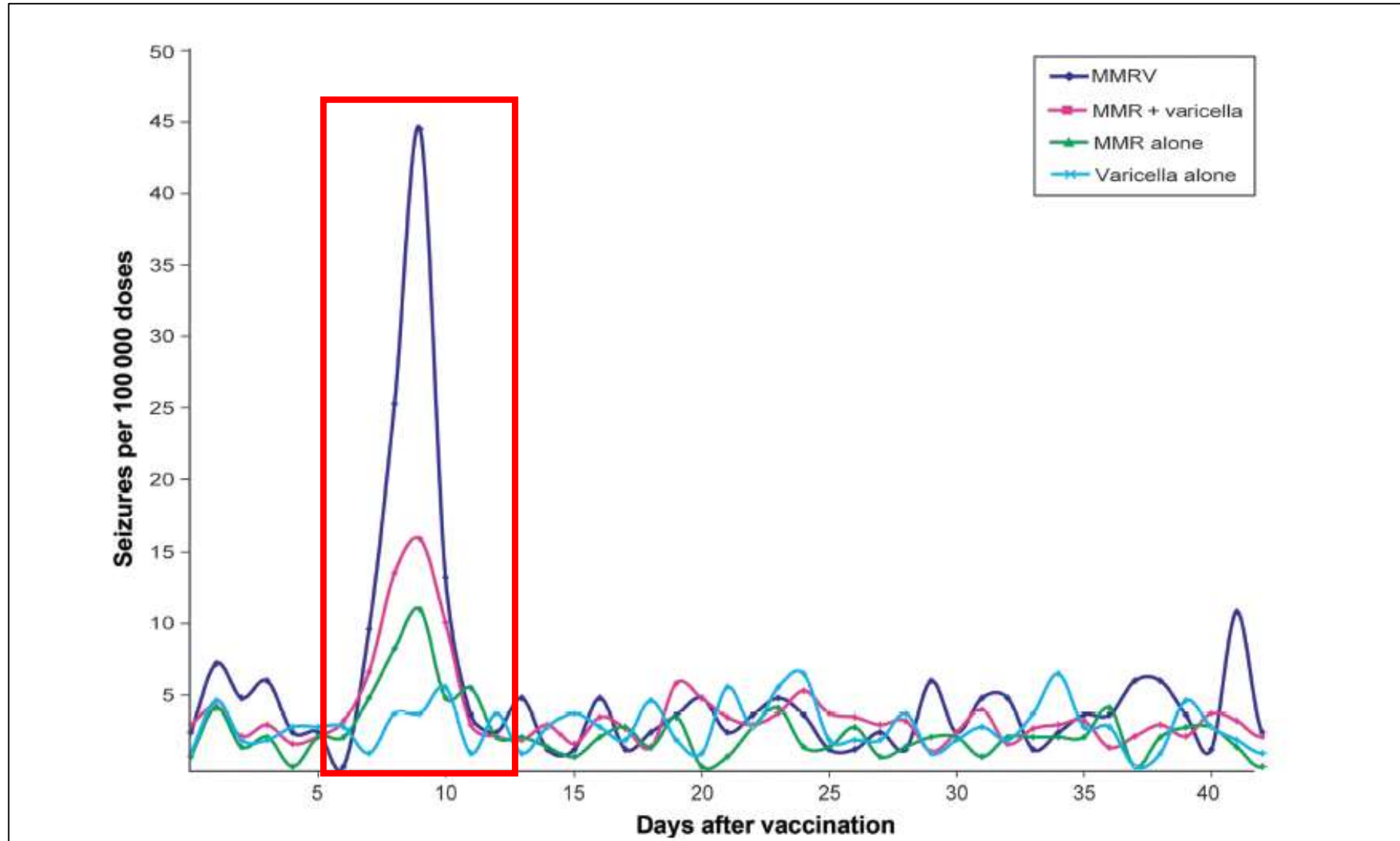
* $p = 0.37$.

† $p = 0.26$ (chi-squared test of the comparison across doses).

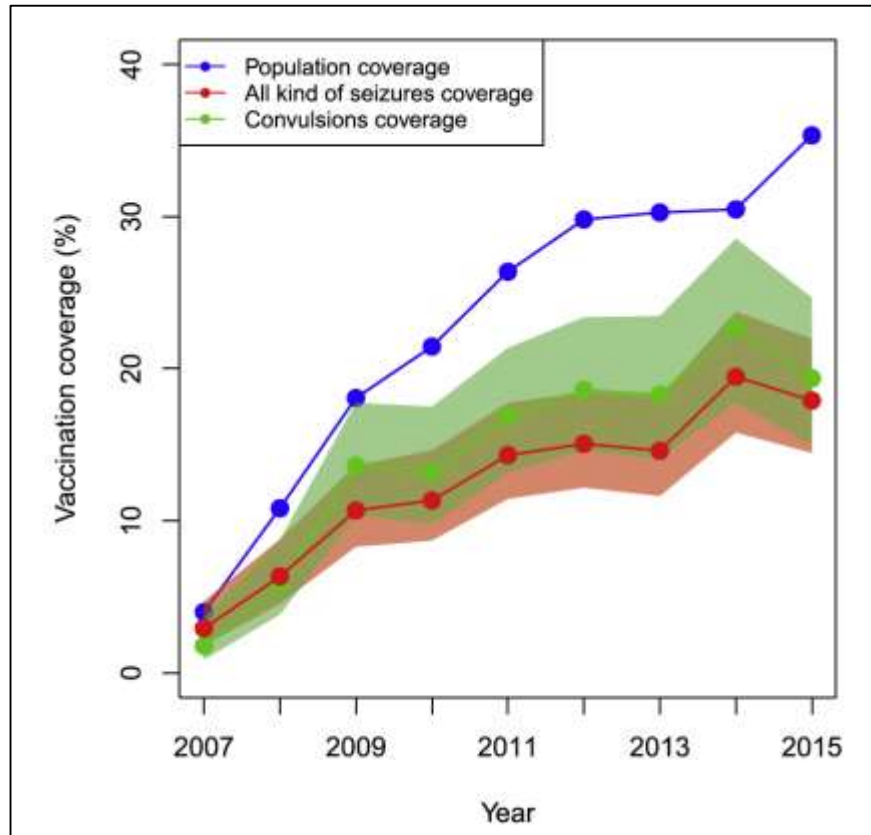
Complications neurologiques de la rougeole : les encéphalites



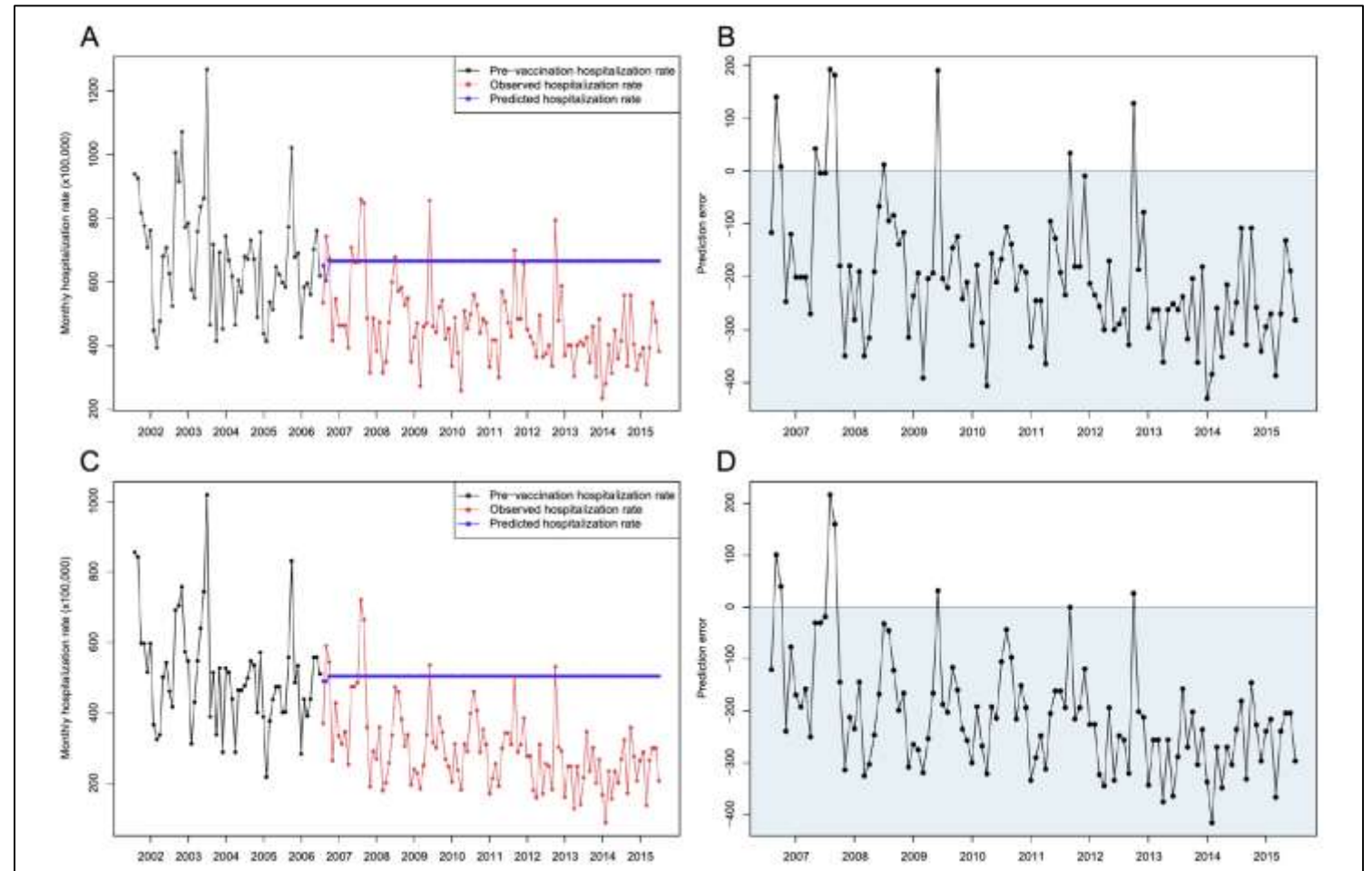
Vaccin combiné rougeole-oreillons-rubéole-varicelle et risque de convulsions fébriles



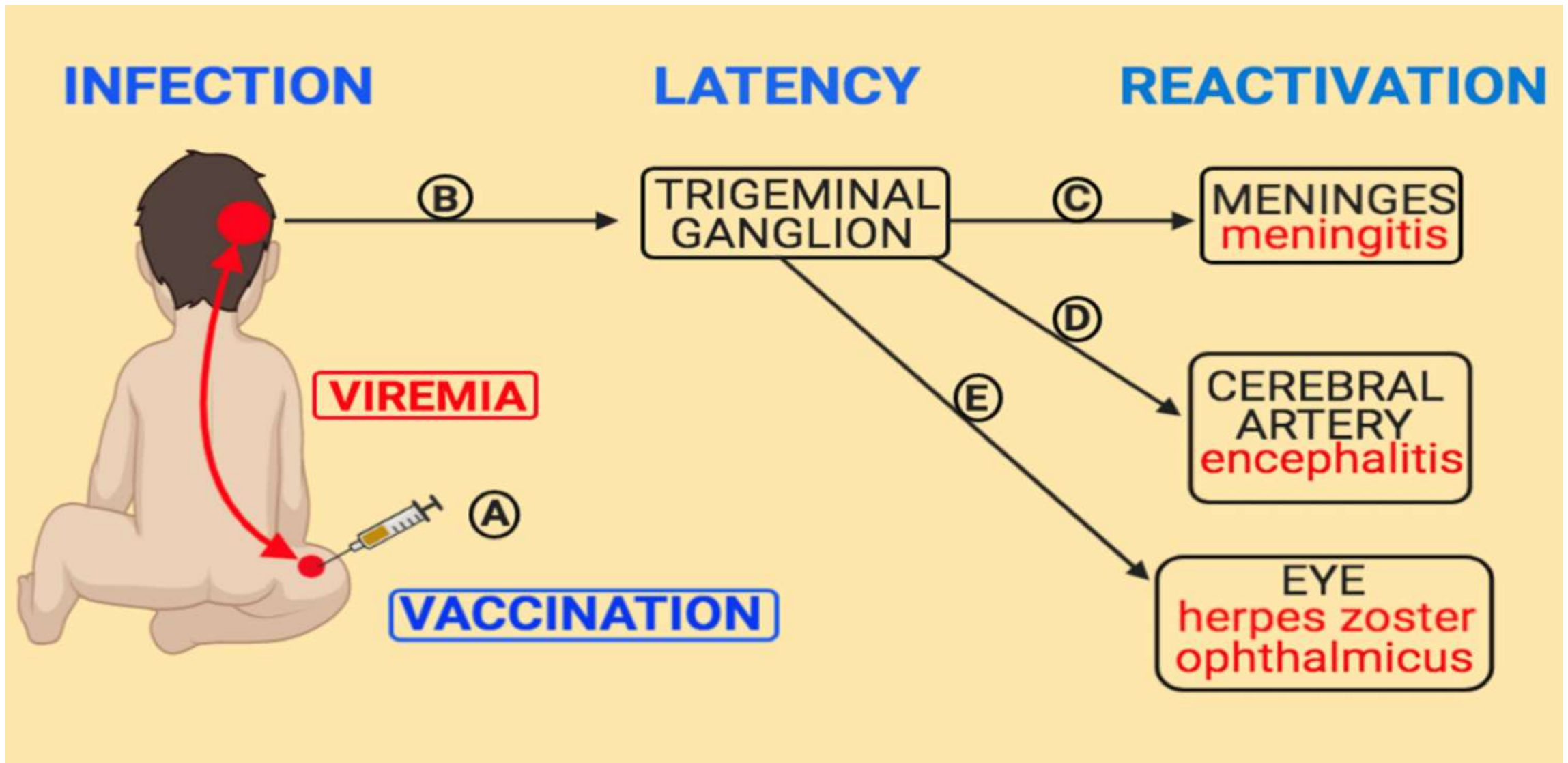
Impact de la vaccination contre le rotavirus sur les hospitalisations infantiles pour convulsions



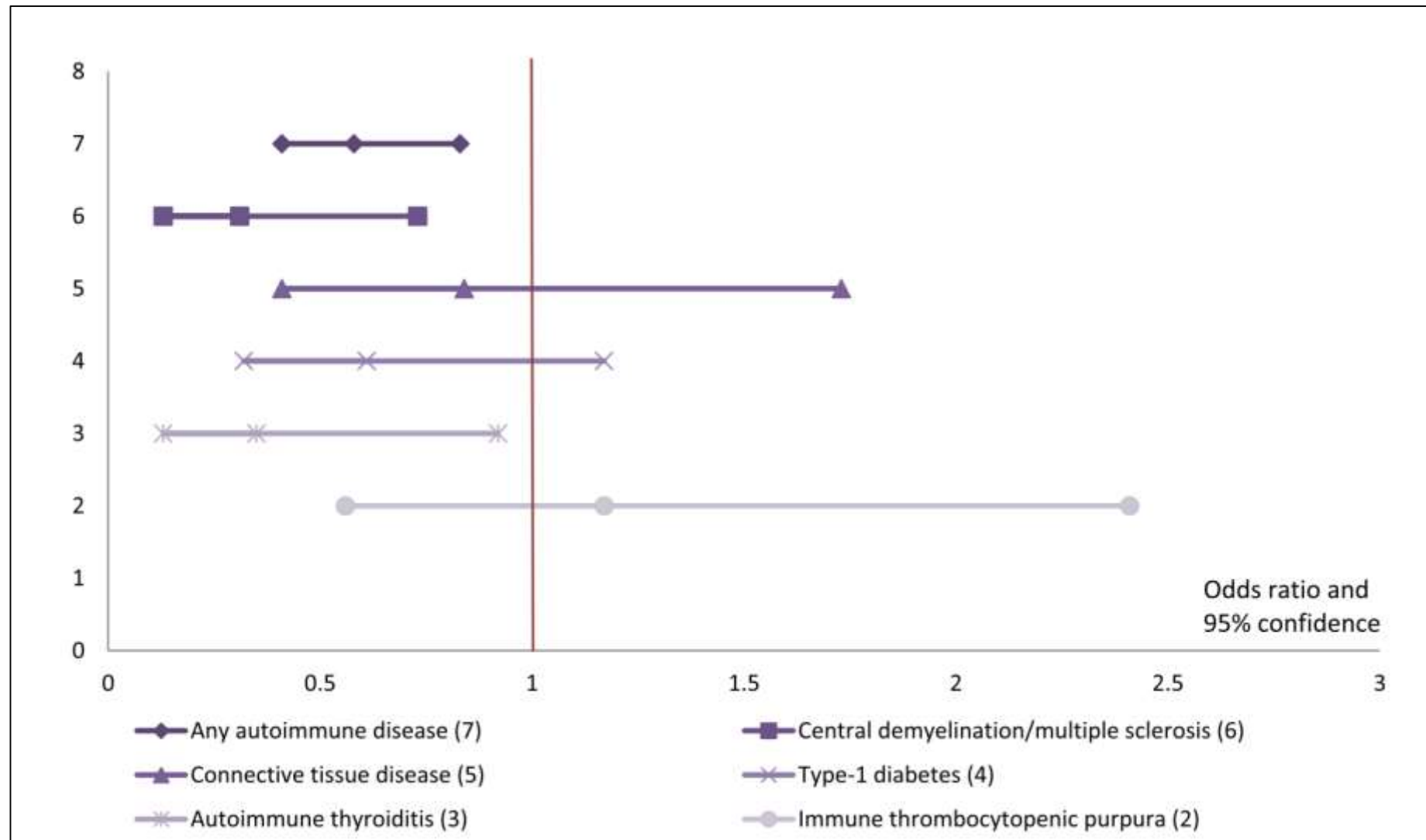
A. Salas et al. / Vaccine 37 (2019) 3362–3368



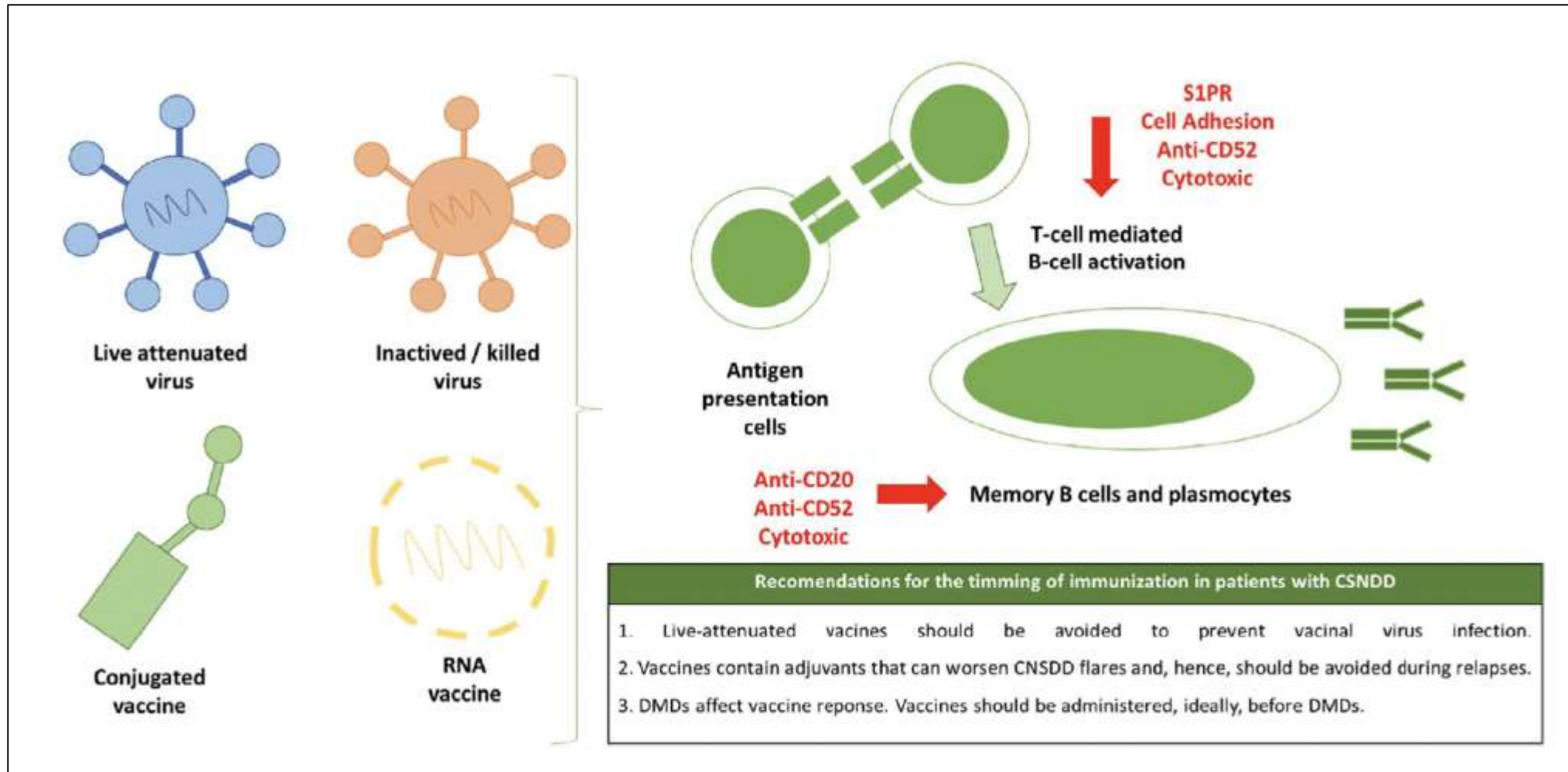
Méningite après la vaccination contre la varicelle



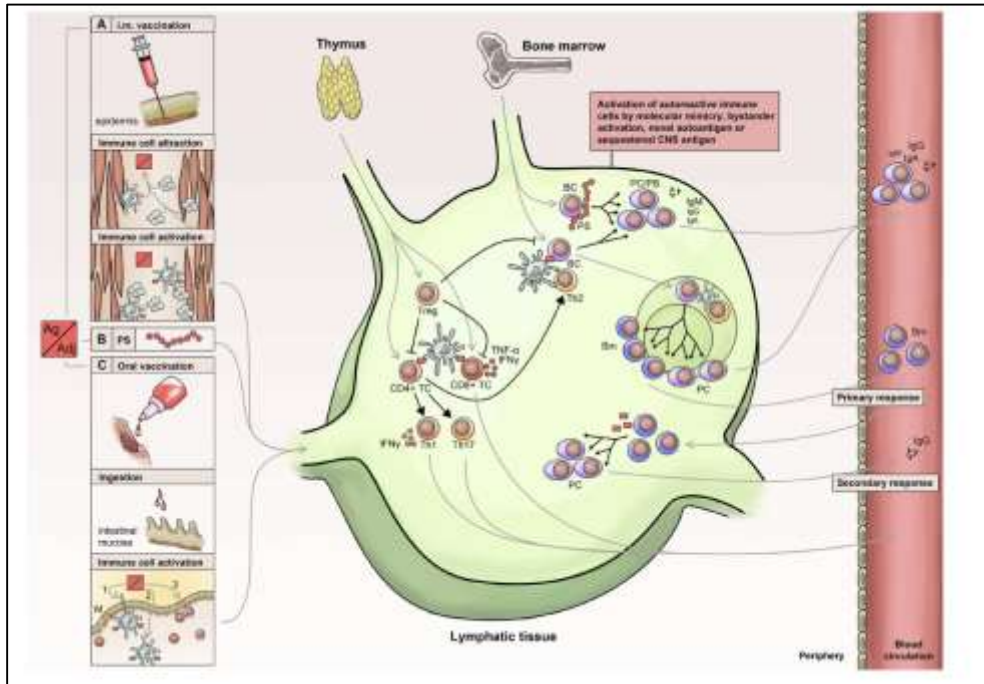
Risque de maladies auto-immunes et vaccins anti-HPV six ans de surveillance



Défis et perspectives en matière de vaccination chez les patients atteints de maladies démyélinisantes



Vaccination dans la sclérose en plaques : Ami ou Ennemi ?



Frontiers in Immunology | www.frontiersin.org
1 August 2019 | Volume 10 | Article 1883

Vaccine		USA (CDC/ACIP) (66)	Germany (STIKO) (67)	Recommendation for multiple sclerosis
Diphtheria	Toxoid	All individuals	All individuals	Considered safe
Human papilloma virus	recombinant vaccine	All individuals 11-12a	All individuals 9-14a	Probably safe
Measles, mumps and rubella	live attenuated vaccine	All children and at-risk adults	Unprotected individuals and children exposed to kids	Probably safe, CAVE: Immunosuppression
Meningococcal A,C,W,Y	inactivated vaccine	At-risk individuals	At-risk individuals	Probably safe
Meningococcal B	recombinant vaccine	At-risk individuals	At-risk individuals	Probably safe
Pertussis	Toxoid	All individuals	All individuals	Probably safe
Pneumococcus	polysaccharide vaccine	All individuals > 65a and individuals at risk	All individuals > 60a and individuals at risk	Insufficient data
Tetanus	Toxoid	All individuals	All individuals	Considered safe
Varicella	live attenuated vaccine	Individuals lacking evidence of immunity	Seronegative individuals at risk	Probably safe, CAVE: Immunosuppression
Zoster	recombinant vaccine	All individuals > 50a	All individuals > 60a and individuals > 50 at risk	Insufficient data
Zoster	live attenuated vaccine	All individuals > 60a, recombinant preferred	Not recommended	Insufficient data, CAVE: Immunosuppression
Hepatitis B	recombinant vaccine	All children, individuals not at risk but who want protection from hepatitis B	All children, individuals at risk	Considered safe
Hepatitis A	inactivated vaccine	All children, individuals not at risk but who want protection from hepatitis A	All children, individuals at risk	Considered safe
Poliomyelitis	inactivated vaccine	All children	All children, individuals at risk	Considered safe
Haemophilus influenzae type b	Conjugate vaccine	All children, individuals at risk	All children, individuals at risk	Insufficient data
Tick-borne encephalitis	Inactivated vaccine	not available	Endemic areas and tick exposure	Probably safe
Yellow fever	live attenuated vaccine	endemic areas	endemic areas	Probably increased risk, CAVE: Immunosuppression
Rabies	inactivated vaccine	People at high risk of exposure	People at high risk of exposure	Considered safe
Influenza	inactivated vaccine	All individuals > 6 months	Individuals >65 years old, those with chronic diseases, and pregnant women	Considered safe
Influenza	live attenuated vaccine	Individuals 2a-49a with restrictions	Individuals w/ chronic disease 2-17a, inac. preferred	Not recommended

Risque des différents vaccins dans le déclenchement de la SEP

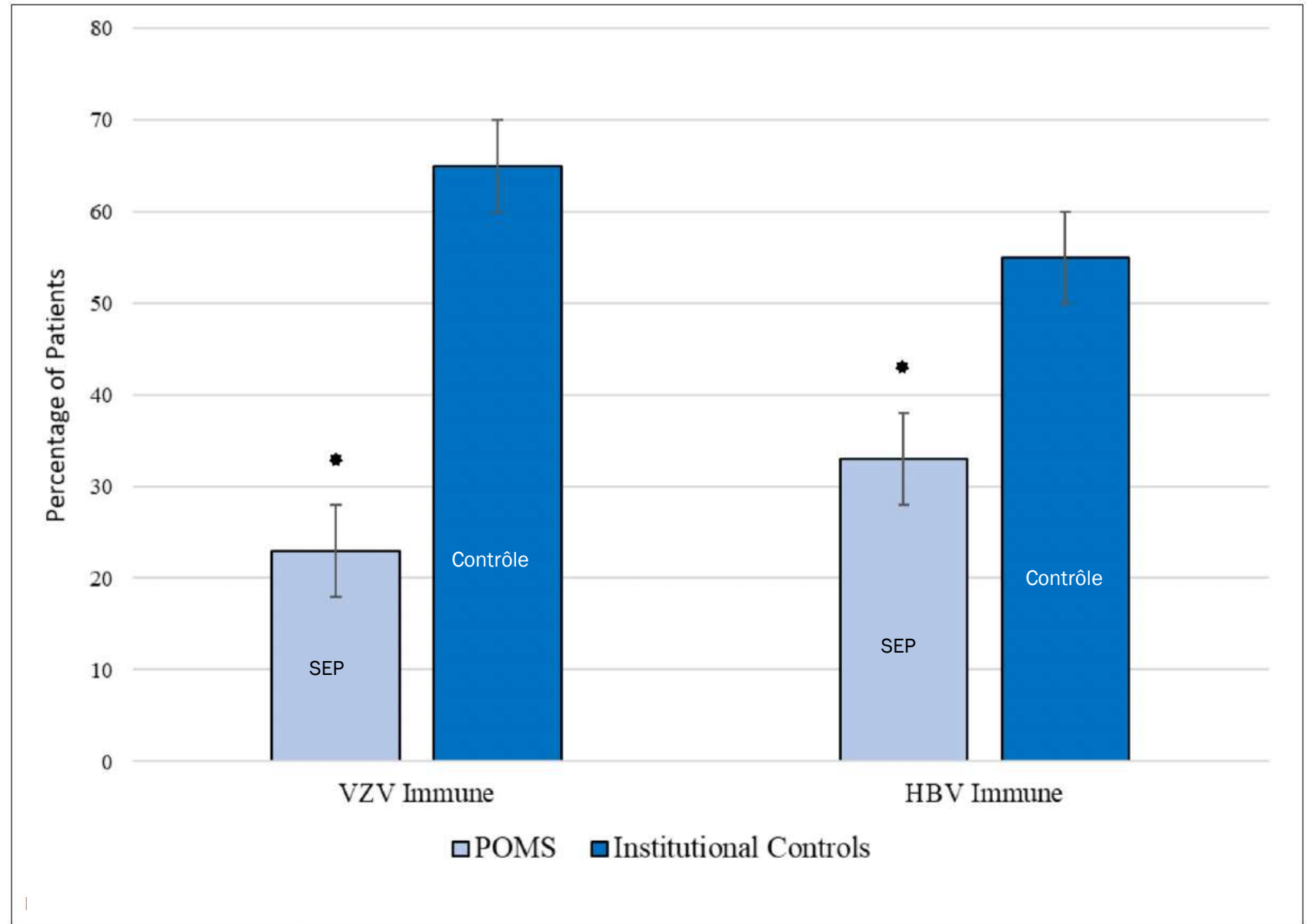
Méta-analyses

Vaccinations	Nombre d'études	Nombre total de cas/témoins	Odds-ratio (IC ₉₅)	PI ₉₅
BCG	6	536/751	0,96 (0,69-1,34)	0,60-1,54
Diphtérie	3	237/387	0,60 (0,40-0,91)	0,04-8,57
Hépatite B	6	15 241/12 339	1,00 (0,74-1,37)	0,45-2,26
Grippe	4	14 997/10 128	0,97 (0,77-1,23)	0,42-2,23
RRO	3	568/1880	1,02 (0,64-1,62)	0,05-20,58
Poliomyélite	7	570/725	0,87 (0,61-1,26)	0,39-1,98
Tétanos	8	929/3 203	0,71 (0,57-0,88)	0,47-1,07
Fièvre typhoïde	4	288/467	1,05 (0,72-1,53)	0,37-3,01

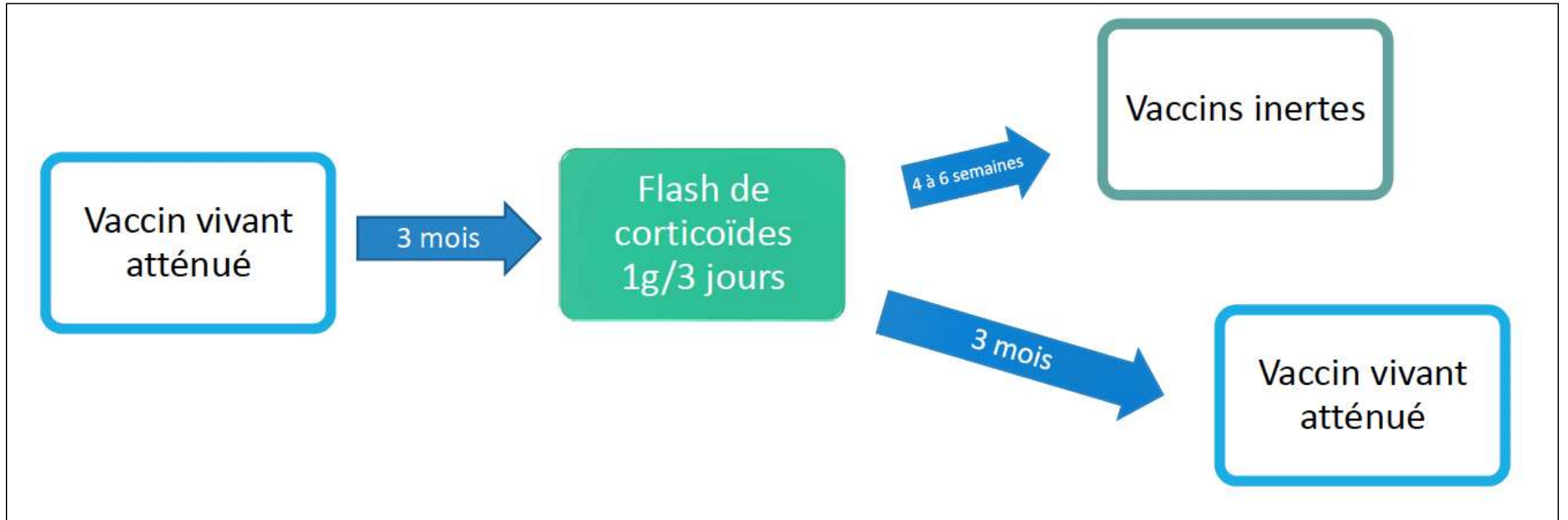
PI: Prediction Interval.

Réponses vaccinales inadéquates chez les enfants atteints de sclérose en plaques

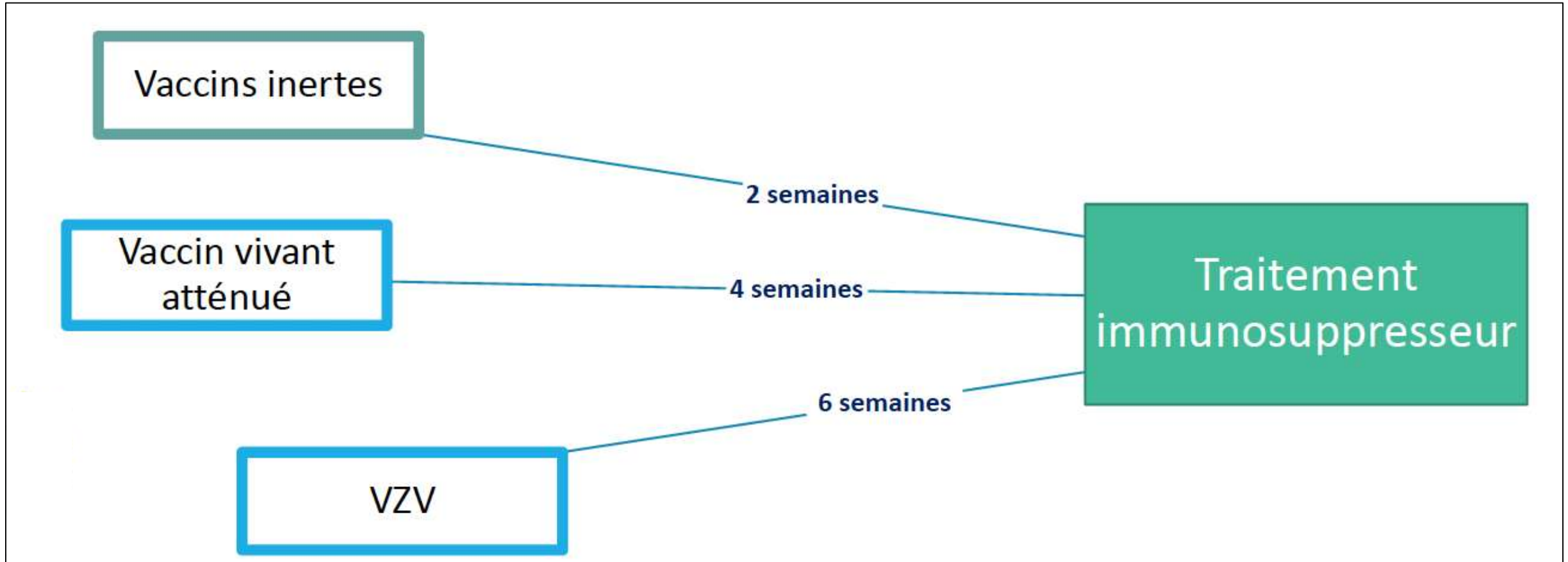
Frontiers in Pediatrics | www.frontiersin.org 1
December 2021 | Volume 9 | Article 790159



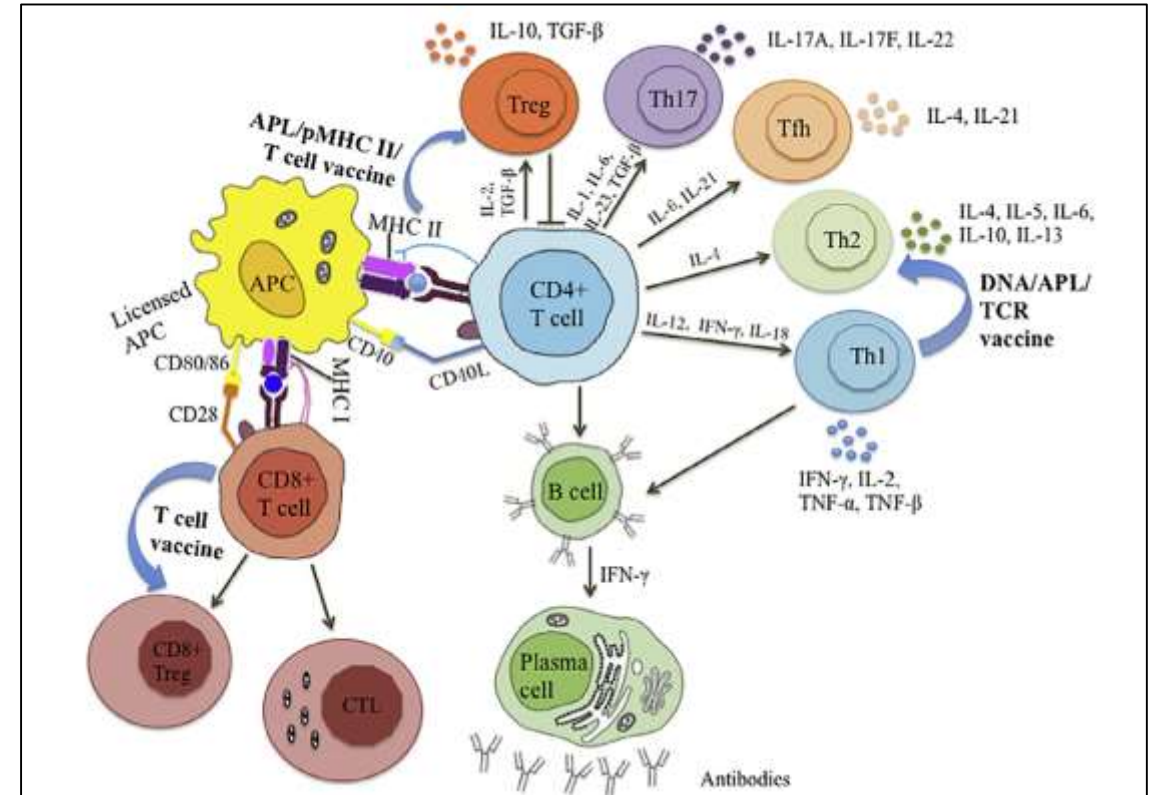
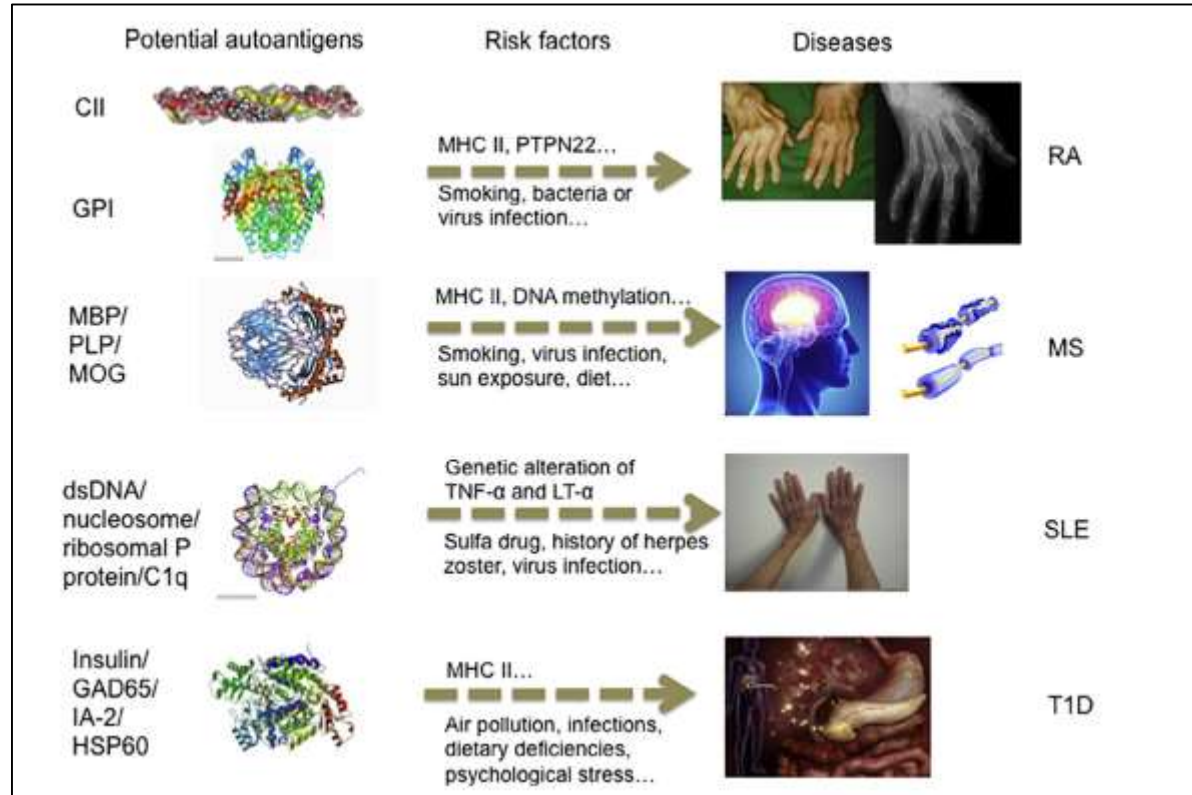
Vaccin et flash de corticoïdes



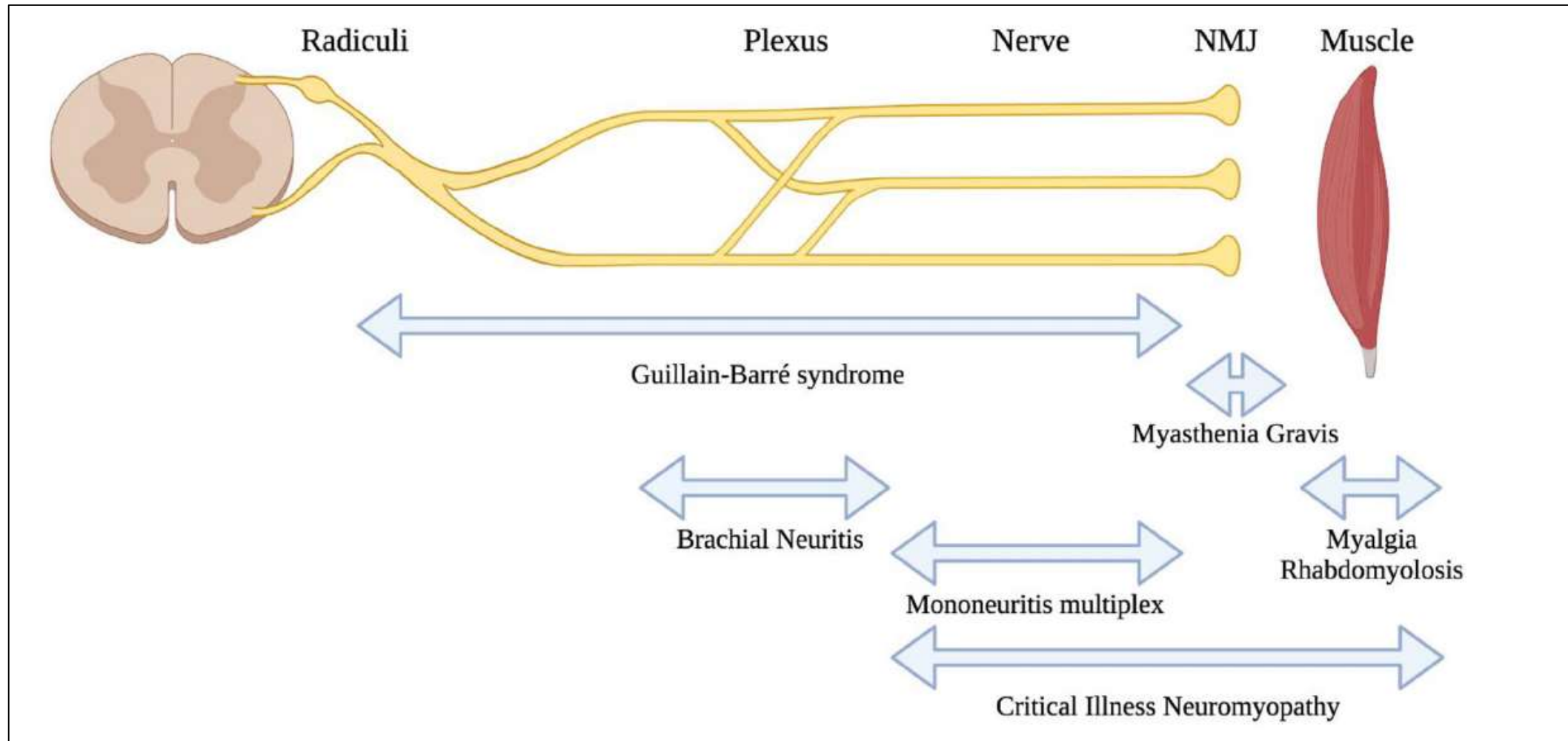
Avant traitement immunosuppresseur



Progrès récents dans le développement de vaccins contre les maladies chroniques et auto-immunes inflammatoires



Complications neuro-musculaires de SRAS-CoV-2 et autres infections virales

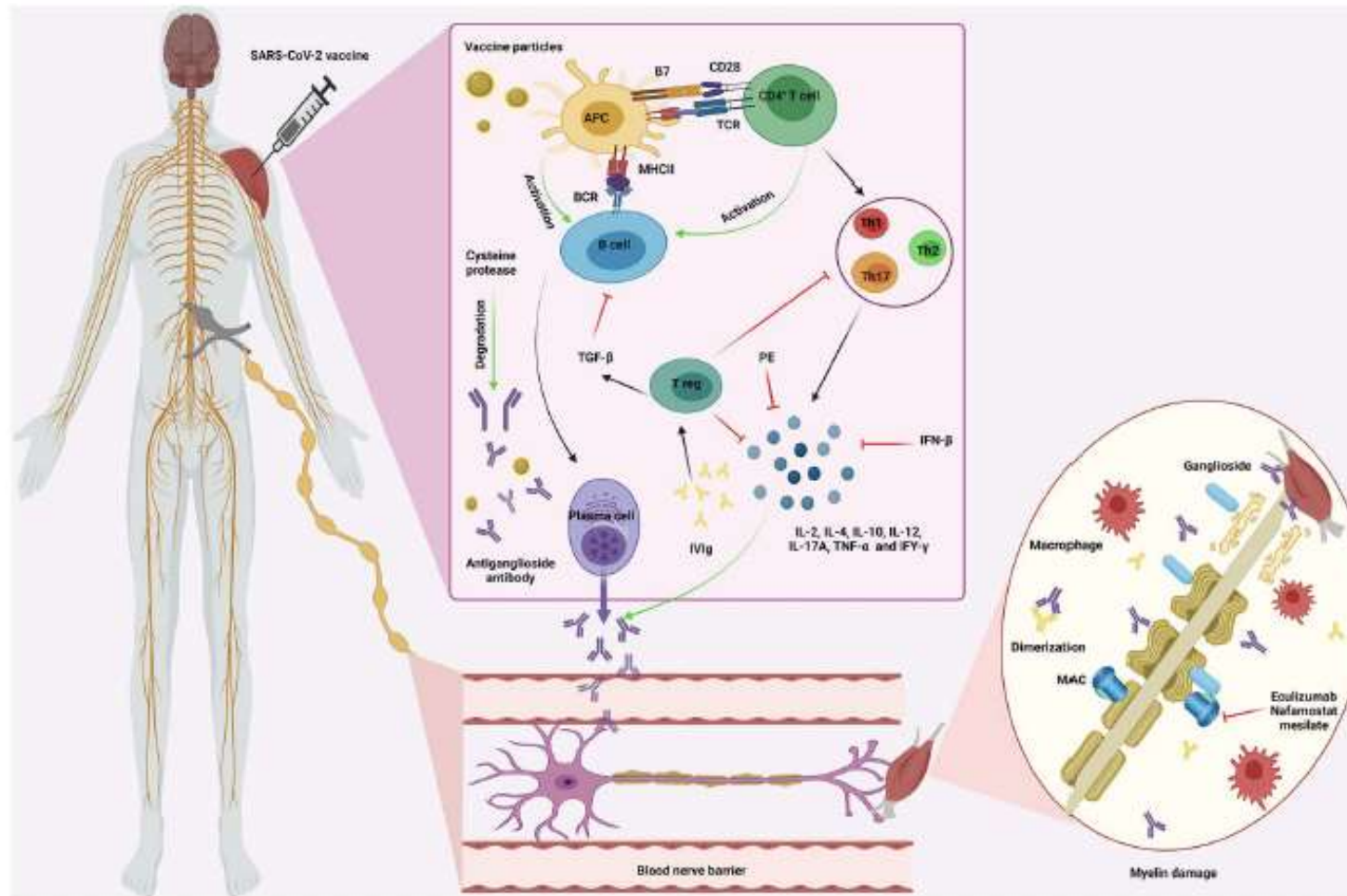


Vaccination COVID-19 dans les maladies auto- immunes : Innocuité des vaccins dans les myopathies inflammatoires idiopathiques

Muscle & Nerve. 2022;66:426-437.

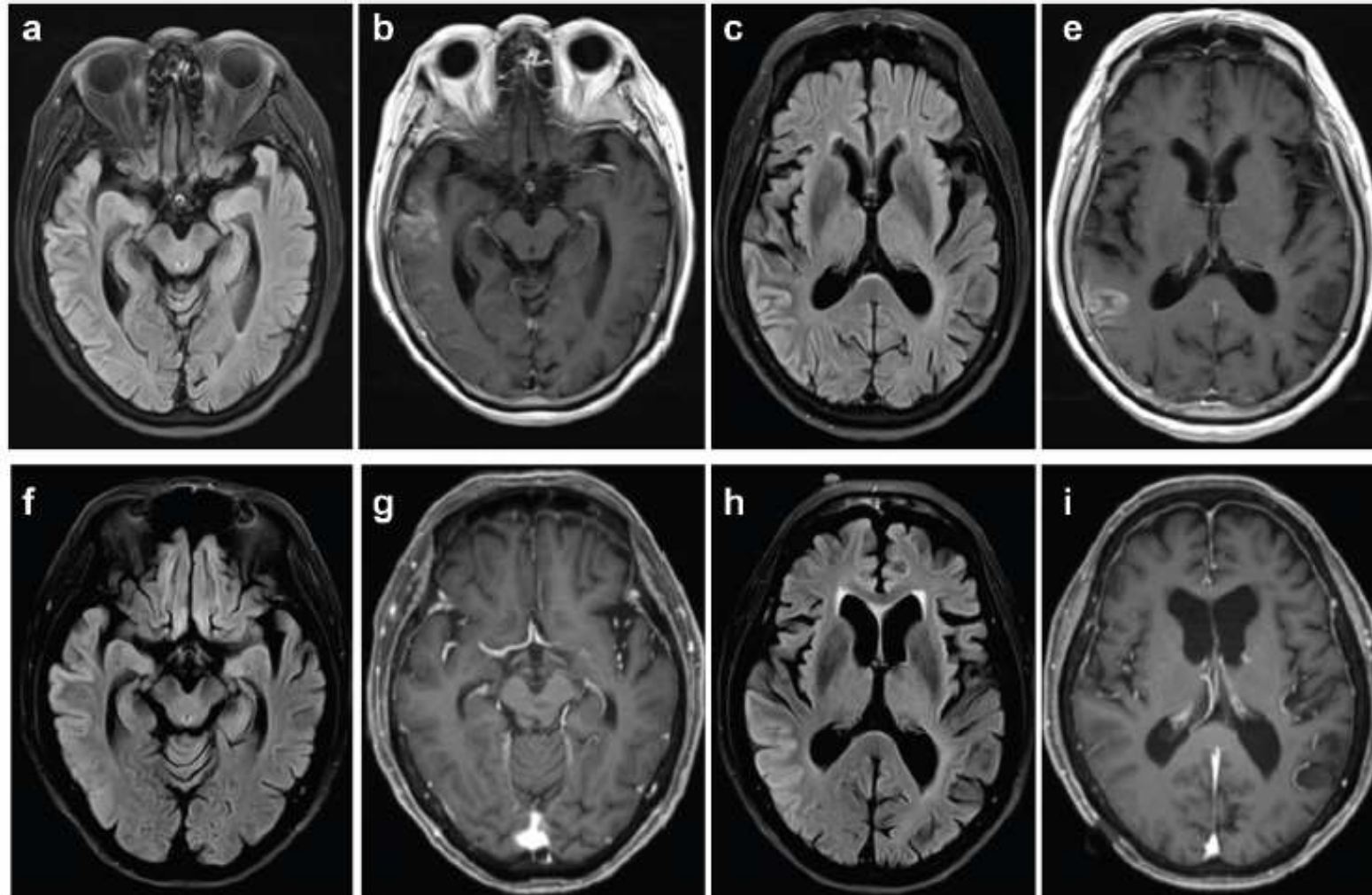
	IIMs ^a (n = 1227)	Other SAIDs ^a (n = 4640)	HCS ^a (n = 5033)	OR 1 (CI)	OR 2 (CI)	P1	P2
Injection-site pain	784 (63)	3036 (65)	3138 (62)			.316	.365
Minor ADEs							
Myalgia	144 (12)	777 (17)	778 (15.5)	0.6 (0.5-0.8)	0.7 (0.6-0.8)	<.001	<.001
Body ache	233 (19)	1067 (23)	1082 (21)	0.8 (0.7-0.9)		.003	.055
Fever	151 (12)	863 (18)	960 (19)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	<.001	<.001
Chills	176 (14)	714 (15)	631 (12.5)			.365	.104
Nausea and vomiting	74 (6)	311 (7)	222 (4.4)		1.3 (1-1.8)	.398	.021
Headache	271 (22)	1290 (28)	1125 (22.4)	0.7 (0.6-0.8)		<.001	.884
Rashes	34 (3)	91 (2)	48 (1)		2.9 (1.8-4.5)	.081	<.001
Fatigue	348 (28)	1511 (32)	1359 (27)	0.8 (0.7-0.9)		<.001	.395
Diarrhea	29 (2.4)	174 (4)	120 (2.4)	0.6 (0.4-0.9)		.018	.945
Abdominal pain	27 (2)	126 (3)	72 (1.4)			.314	.059
High pulse rate or palpitations	27 (2)	166 (4)	125 (2.5)	0.6 (0.4-0.9)		.016	.527
Rise in blood pressure	8 (0.6)	65 (1)	47 (0.9)	0.5 (0.2-0.9)		.035	.328
Fainting	4 (0.3)	23 (0.5)	16 (0.3)			.435	.980
Difficulty in breathing	10 (0.2)	59 (1)	50 (1)			.187	.543
Dizziness	58 (4.8)	291 (6)	229 (4.4)	0.7 (0.5-0.99)		.042	.498
Chest pain	17 (1.4)	81 (2)	60 (1.2)			.381	.611
Others	77 (6)	431 (9)	270 (5)			.567	.247
Major ADEs							
Anaphylaxis	5 (0.4)	6 (0.1)	5 (0.1)		5 (1.3-19)	.060	.070
Marked difficulty in breathing	9 (0.7)	27 (0.6)	27 (0.5)			.545	.430
Throat closure	4 (0.3)	23 (0.5)	4 (0.3)			.435	.167
Severe rashes	10 (0.8)	31 (0.7)	15 (0.3)		2.7 (1.2-6)	.583	.011
Others	40 (3)	149 (3)	56 (1)		2.9 (1.9-4.4)	.945	.042
Hospitalization	7 (0.6)	20 (0.4)	11 (0.2)		2.5 (1-6.7)	.521	.042

Un examen des événements indésirables neurologiques potentiels des vaccins de la COVID-19

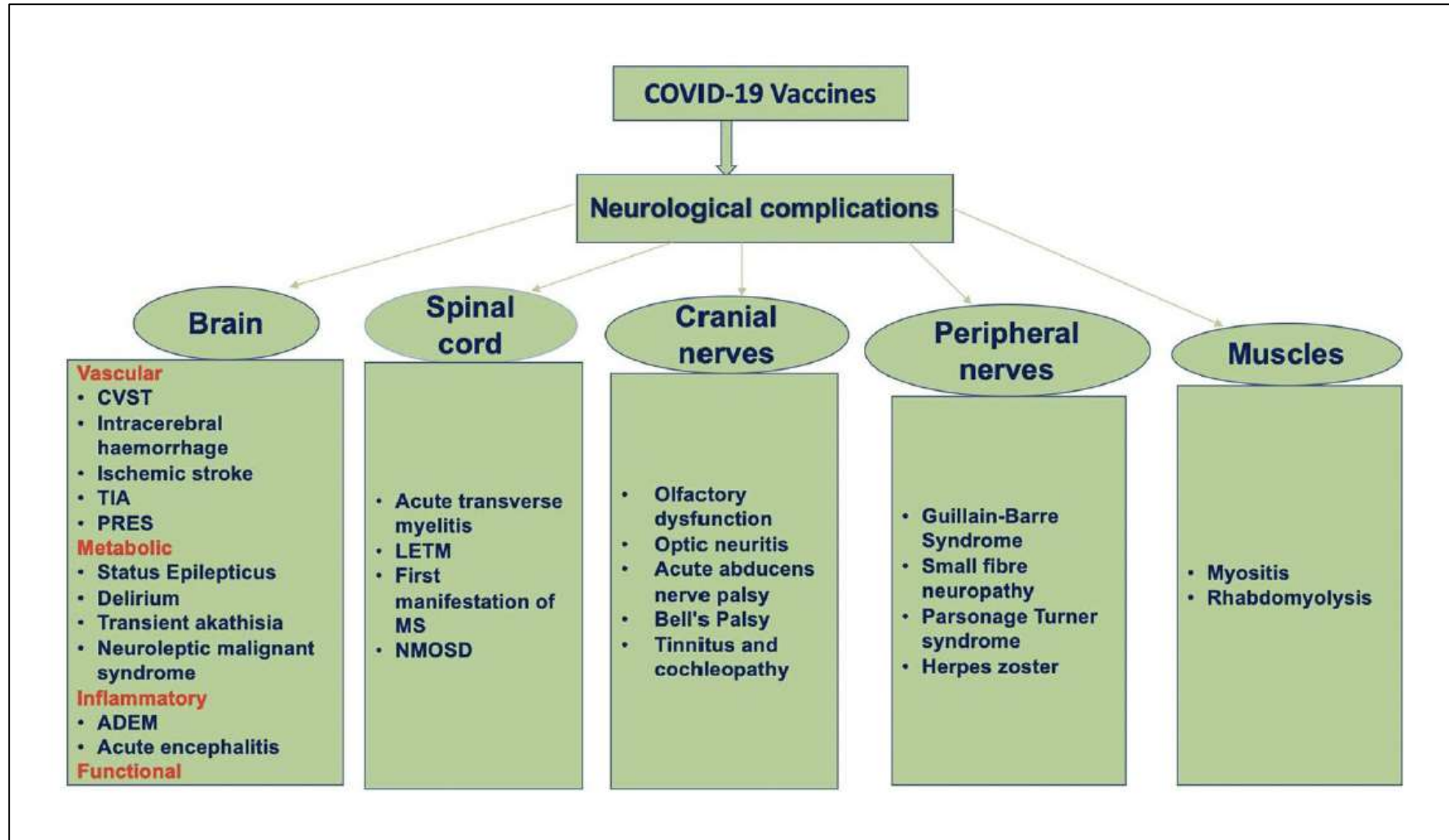


Encéphalite aiguë après vaccination COVID-19

Rapport de cas et revue de la littérature



Vaccination anti-COVID-19 Spectre des complications neurologiques



Syndrome vaccinal long post-COVID

Brain Nerves, 2022
doi: 10.15761/JBN.1000133



Mental Health

- Anxiety
- Depression
- Sleep problems
- Substance abuse



Respiratory System

- Cough
- Low blood oxygen
- Shortness of breath



Kidney

- Acute kidney injury
- Chronic kidney disease



Gastrointestinal

- Diarrhea
- Acid reflux
- Constipation



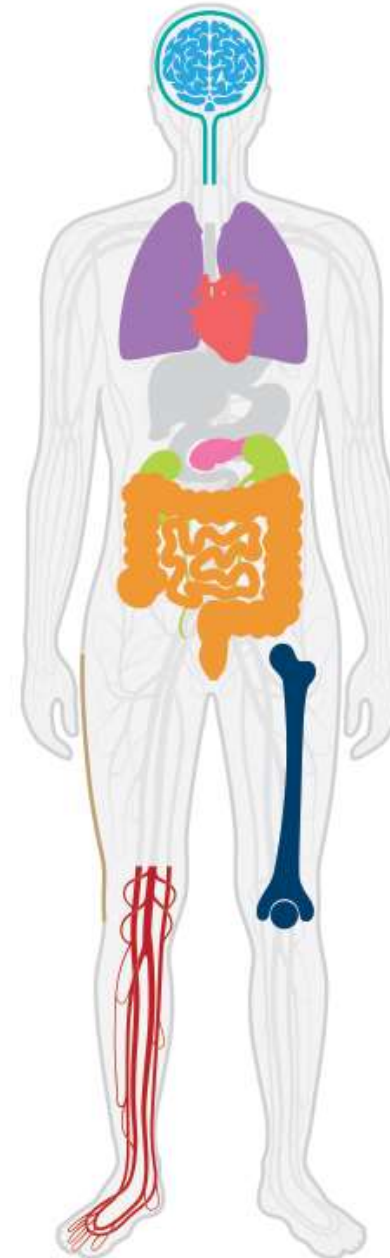
Skin Disorders

- Rash
- Hair loss



Blood Disorders

- Anemia
- Blood clots



Nervous System

- Stroke
- Headaches
- Memory problems
- Loss of smell and taste



Cardiovascular

- Arrhythmia
- Palpitations
- Heart failure
- Acute coronary disease



Metabolic/Endocrine

- Obesity
- Diabetes
- High cholesterol



Musculoskeletal

- Joint pain
- Muscle weakness



General

- Fatigue
- Malaise
- Mitochondrial dysfunction