



A NEW PERSPECTIVE IN DENGUE PREVENTION: FROM CLINICAL DEVELOPMENT TO REAL-WORLD PRACTICE

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Most hospitalizations and severe dengue after secondary infections^{1,2}

Serotype of DENV infection	Proportion of infections that proceed to disease outcome during follow-up, % (95% CI)								
	Symptomatic VCD (2 Year)	Hospitalized VCD (5 Year)	Severe VCD (5 Year)						
DENV-1	48.7 (43.5, 53.8)	3.4 (2.2, 4.8)	0.5 (0.1, 1.1)						
DENV-2	55.3 (51.4, 59.8)	12.7 (11.6, 14.0)	2.6 (2.0, 3.2)						
DENV-3	30.5 (27.1, 34.4)	3.3 (2.6, 3.9)	1.0 (0.7, 1.4)						
DENV-4	30.5 (27.1, 34.4)	3.3 (2.6, 3.9)	1.0 (0.7, 1.4)						
>85% of hospita	lizations and sever	e disease in seroposi	itive individuals						
CI, confidence interval; DENV, dengue virus; VCD, virologically confirmed dengue. Sam Clifford and Stefan Flasche LSHTM, personal communication. 1. Sridhar S, et al. <i>N Engl J Med</i> 2018;327–340; 2. Flasche S, et al. <i>Plos Med</i> 2016;12::1002181									

Vaccine-Preventable Infections in Travellers:	^{100%}
Incidence per Month	1 1
COVID-19, anecdotal data from cruise ships	10% = 1 / 10
Influenza, symptomatic with seroconversion Dengue, symptomatic with seroconversion Animal bite — rabies risk	- <u> </u>
Yellow fever, Ilha Grande outbreak 2016 Yellow fever, West Africa	0.1% = 1/1,000
Typhoid, South Asia Yellow fever, South America Hepatitis A, Africa Tick borne encephalitis, rural Baltics	 0.01% = 1/10,000
Measles Hepatitis A, Asia Hepatitis B, Asia Active tuberculosis, U.S. Peace Corps Volunteers Hepatitis A, Lotin America Typhoid, Africa, Latin America, Middle East, SE-Asia	0.001% = 1/100,000
Pertussis	 0.0001% = 1/million
Steffen R et al. J Travel Med. 2023 Japanese encephalitis Cholera Rabies, fatal Meningococcal Disease Diphtheria Poliomyelitis Tetanus	

Table 2. Demographic Characteri Medical History of Patients With C Reported to GeoSentinel 2007-2	stics, Travel Deta Complicated Den 022 (n = 86)	ils, and gue
Characteristic	Available Data	Missing
Demographic characteristic		
Median age (range), v	34 (8-91)	-
Female, n (%)	48 (56)	-
Travel history, n (%)		
Region of exposure	86 (100)	-
Caribbean	27 (31)	
Southeast Asia	21 (24)	
Oceania	11 (13)	
Sub-Saharan Africa	10(12)	
South America	9 (11)	
South Central Asia	8 (9)	
Reason for travel	85 (99)	1(1)
Tourism	39 (46)	
Visiting friends and relatives	27 (32)	
Business	10(12)	
Humanitarian aid/missionary/ volunteer	6 (7)	
Student study abroad	2 (2)	
Expatriate	1 (1)	-
Duration of travel	86 (100)	-
<2 wk	25 (29)	
≥2 to <4 wk	33 (38)	
≥4 to <12 wk	17 (20)	
≥12 wk	11 (13)	

ן Sentinel study; 5,958	oatient	ts with den
$0 \mathbf{F} \left(2 0 \right) $		
95 (2%) complication	ated de	engue
		8
Madical history = (%)		
Comorbiditios*	84 (09)	2(2)
Any comorbidity	21 (25)	2(2)
Hypertension	7 (33)	
Diabetes	5 (23)	
Rheumatologic disease	4 (19)	
Chronic respiratory disease	3(14)	
Obesity	3 (14)	
Cancer	2 (10)	
Congestive heart failure	2 (10)	
Neurologic disease	2 (10)	
Chronic kidney disease	1 (5)	
Vaccination history	48 (56)	38 (44)
Any flavivirus vaccine	23 (48)	
Yellow fever vaccine data	22 (96)	1 (4)
Vaccine received	19 (86)	
Tickborne encephalitis vaccine data	20 (87)	3 (13)
Vaccine received	3 (15)	
Japanese encephalitis vaccine data	21 (91)	2 (9)
Vaccine received	5 (24)	
Prior dengue virus infection		
Based on history		
Yes	6(7)	
No	57 (66)	
Unknown	23 (27)	
Based on serology†	44 (51)	42 (49)
Primary dengue virus infection	32 (73)	
Secondary dengue virus infection	12 (27)	

Table 1	I. Overvi	ew of	published cas	es of import	ed dengue with fatal o	outcomes (n=	9)					
Year Gender	Age	Country of residence	Country of dengue acquisition	Cause of Death	Time of death (DPSO)days	Dengue diagnosis and serotype		Primary/Secondary dengue infection			Rcf.	
										IgM	IgG	
1998	F	25	Netherlands	Thailand	Cerebral edema	6	RT- PCR	DENV-3	Prim.	1/128	1/16	20
2002	F	32	Finland	SE Asia	Cerebral hemorrhage	37	PRNT	DENV- 1/2	Prim.	POS	NEG	13
2005	F	28	USA	Mexico	-	-	-	-	-	-	-	18
2005	F	30	Norway	Mexico	Subarachnoid hemorrhage	8	RT- PCR	DENV-2	Prim.	POS	NEG	14
2008	F	50	Norway	Thailand	DSS	7	RT- PCR	DENV-1	Prim.	POS	NEG	15
2009	М	54	Netherlands	Saint Martin	DSS	4	RT- PCR	DENV-2	Prim.	NEG	NEG	16
2009	F	21	Germany	Ecuador	Postoperative hemorrhage	11	RT- PCR	DENV-1	Sec.	1/20	1/2560	17
2012	F	63	USA	USA	Hemophagocytic lympho- histiocytosis	38	RT- PCR	DENV-3	Prim.	POS	-	19
2015	F	34	Australia	Papua New Guinea	Myocarditis/cerebral edema	6	RT- PCR	DENV-3	Prim.	POS	NEG	21





- All travellers are at risk no specific behaviour or destination
- Rate of asymptomatic cases is unknown
- Reasons for complications are not clear
- Complications increase with 2nd infection,
- > Many cases develop during travel, and are treated there
- > Tt is symptomatic, monoclonals may be game changers
- > An effective protection against dengue is important
- > Current advice to travelers to dengue endemic regions:
 - Avoid travel (unrealistic)
 - Mosquito bite protection (incomplete)

Vaccination (?)

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Impact and Incidence of Vaccine-Preventable Diseases in Travelers

Impact VERY HIGH: CFR > 10% and/or Frequent sequelae	 Japanese encephalitis Rabies Meningococcal disease Diphtheria Poliomyelitis Tetanus 			Yellow fever, South America	 Yellow fever: in outbreak West Africa
HIGH: CFR 1-10% <i>and/or</i> Sequelae			 Tick-borne encephalitis, rural Baltics 		
INTERMEDIATE: CFR ± 1% and Hospitalization > 10%	 Typhoid: NE- Asia, Caribbean Cholera 	 Typhoid: Africa, Latin America, Middle East, SE-Asia Pertussis 	 Hepatitis A Hepatitis B Measles 	 Typhoid: South Asia 	• Dengue
LOW: CFR < 1% and Hospitalization < 10%		Pertussis		• Mpox (?)	COVID-19 Influenza [Risk of rables, PEP indicated]
	< 0.1	0.1-0.9 Incidence per 1	1-9 00,000 person-	10-99 months	≥ 100
BCRT		Steffen R et	al. J Travel M	Med. 2023	















information_en.pdf (accessed February 2024).

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Most frequent unsolicited AEs were nasopharyngitis (2.6%) and upper respiratory tract infection $(2.3\%)^1$

Most frequent TAK-003-related unsolicited AEs were injection-site pruritus (0.7%), bruising (0.7%), and pyrexia (0.8%)¹

Fever occurred in 8.9% after any dose¹

Rash was an uncommon AE $(\geq 1/1000 \text{ to } < 1/100)^2$

Tolerability of the Dengue Vaccine Qdenga® in German Travellers: a prospective survey

Total number pre-travel visits at BCRT from Feb 2023-Feb 2024: 111,059

Doses Qdenga® applied: Female: Male: Undefined: Age Range: Age Average (Median)	26,032 (2 13,384 (5 11,255 (4 1,393 (5 4-79y 34.7y (32y)	23.4%) 51.4%) 44.2%) 5.4%)	1855 Swiner Bremei, 4056 feld Magdebu,	
			1083 ^{ef} Deutschland 1639	
First Vaccination:15,59Second Vaccination:10,43	9 (59.9%) 3 (40.1%)	-	1967 499 urg Mannheim Nürnberg Pisen T: 1564 Presenturg	
Agreed being contacted: 1 Declined: 1	3,845 (53.2%) 2,187 (46.8%)		Straßburg Freiburg im Breisgau Zürich Basel Karzbefehle Karzbefehle Karzb	
BCRT			Source: Tomas Jelinek. Data on File	



Tolerability of the Vaccine Qdenga® in German Travellers: Adverse events

Local AEs Pain 2521 (47.9%) Swelling 1099 (20.9%) Erythema 1432 (27.2%)	Local AE Yes (any): 2521 (47.9%) No (any): 2728 (51.8%) No answer: 13
Systemic AEs Flu-like Symptoms 1262 (24.0%) Fatigue 2112 (40.1%) Fever (>38.5°C) 465 (8.8%)	Systemic AE Yes (any): 2112 (40.1%) No (any): 3128 (59.4%) No answer: 22
Arthalgia 924 (17.6%) Myalgia 1502 (28.5%) Rash 881 (16.7%) Itching 659 (12.5%) Other 622 (11.8%) U 100 (2.8%)	Picture: T. Jelinek
Headache 198 (3.8%) Tail-end events Relapse Hashimoto Myocarditis (MRT	confirmed) 1
Source: Ton	as Jelinek. Data on

Tolerability of the Vaccine Qdenga® in German Travellers: Adverse Events Duration

	1-3	4-7	8-10	11-14	15-20 e	21-30	30+
Local Pain	1862 (73.9%)	500 (19.8%)	83 (3.3%)	40 (1.6%)	16 (0.6%)	12 (0.5%)	8 (0.3%)
n=2521							
Local Swelling	684 (62.2%)	287 (26.1%)	79 (7.2%)	21 (1.9%)	14 (1.3%)	13 (1.2%)	1 (0.09%)
n=1099							
Local Erythema	705 (49.2%)	438 (30.6%)	150 (10.5%)	62 (4.3%)	48 (3.4%)	16 (1.1%)	9 (0.6%)
n=1432							
Flu-like Symptoms	768 (60.9%)	342 (27.1%)	82 (6.5%)	43 (3.4%)	18 (1.4%)	5 (0.4%)	4 (0.3%)
n=1262							
Fatigue	1309 (61.7%)	524 (24.7%)	147 (6.9%)	81 (3.8%)	29 (1.4%)	24 (1.1%)	8 (0.4%)
n=2122							
Fever (>38.5°C)	372 (80.0%)	53 (11.4%)	20 (4.3%)	8 (1.7%)	6 (1.3%)	4 (0.9%)	2 (0.4%)
n=465							
Arthralgia	560 (60.6%)	238 (25.8%)	62 (6.7%)	31 (3.4%)	19 (2.1%)	11 (1.2%)	3 (0.3%)
n=924							
Myalgia	1003 (66.8%)	345 (23.0%)	75 (5.0%)	41 (2.7%)	22 (1.5%)	11 (0.7%)	5 (0.3%)
n=1502							
Exanthema	334 (37.9%)	330 (37.5%)	109 (12.4%)	62 (7.0%)	29 (3.3%)	12 (1.4%)	5 (0.6%)
n=881							
Itching	326 (49.5%)	217 (32.9%)	63 (9.6%)	38 (5.8%)	7 (1.1%)	5 (0.8%)	3 (0.5%)
n=659	_						
Others	292 (46.9%)	157 (25.2%)	56 (9.0%)	44 (7.1%)	38 (6.1%)	21 (3.4%)	14 (2.1%)
n=622							
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Tolerability of the Vaccine Qdenga® in German Travellers: Adverse Events Severity

	sohr schwach	schwach	mittelstark	stark	cohr stark
	Very weak	Weak	Medium	Strong	Very Strong
Local Pain n=2521	379 (15.0%)	1157 (45.9%)	814 (32.3%)	141 (5.6%)	19 (0.8%)
Local Swelling n=1099	203 (18.5%)	551 (50.1%)	264 (24.0%)	65 (5.9%)	10 (0.9%)
Local Erythema n=1432	198 (13.8%)	611 (42.7%)	407 (28.4%)	166 (11.6%)	36 (2.5%)
Flu-like Symptoms n=1262	46 (3.6%)	279 (22.1%)	539 (4 2 .7%)	289 (22.9%)	105 (8.3%)
Fatigue	65 (3.1%)	552 (26.1%)	862 (4 0 .8%)	487 (23.1%)	138 (6.5%)
Fever (>38.5°C)	27 (5.8%)	79 (17.0%)	196 (42.2%)	104 (22.4%)	56 (12.0%)
Arthralgia	34 (3.7%)	233 (25.2%)	343 (37.1%)	205 (22.2%)	104 (11.3%)
Myalgia	77 (5.1%)	482 (32.1%)	582 (38.7%)	253 (16.8%)	101 (6.7%)
n=1502 Exanthema	57 (6.5%)	180 (20.4%)	270 (30.6%)	234 (26.6%)	135 (15.3%)
n=881	57 (8.6%)	242 (36.7%)	208 (31.6%)	101 (15.3%)	50 (7.6%)
n=659 Others	26 (4.2%)	88 (14.1%)	224 (36.0%)	180 (28.9%)	93 (15.0%)
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Tolerability of the Vaccine Qdenga® in German Travellers: Adverse Events and Co-Vaccination

AEs	Any Other Vaccination n=3,352	No Other Vaccination n=1,892	P-Value
Local Pain	1748 (52.1%)	771 (40.8%)	< 0.01
Local Swelling	729 (21,7%)	381 (20.1%)	n.s.
Local Erythema	936 (27.9%)	510 (27.0%)	n.s.
Flu-like Symptoms	841 (25.1%)	392 (20.7%)	< 0.01
Fatigue	1479 (44.1%)	639 (33.8%)	< 0.01
Fever >38.5°C	342 (10.2%)	128 (6.8%)	< 0.01
Arthralgia	649 (19.4%)	279 (14.7%)	< 0.01
Myalgia	1045 (31.2%)	452 (23.9%)	< 0.01
Rash	618 (18.4%)	278 (14.7%)	< 0.01
Itching	437 (13.0%)	229 (12.1%)	n.s.
Other	408 (12.2%)	211 (11.6%)	n.s.
BCRT		Source: Torr	nas Jelinek. Data on

Tolerability of the Vaccine Qdenga® in German Travellers: Systemic AE and Co-Vaccination

	Co-Vaccination												
AEs	None	Cholera	YF	Flu	Hep A	Hep A+B	Jap. Enc.	MMR	Men ACWY	Polio	TdapP	Rabies	Typhoid
Flu-like	392	45	122	27	72	29	214	8	49	30	49	423	229
Symptoms	(20.7%)	(20.4%)	18.9%	25.2%	22.4%	(16.8%)	(28.7%)	(17.4%)	(31.4%)	25.6%	(36.3%)	(27.9%)	(25.6%)
Fatigue	639	87	250	40	138	58	363	16	74	49	68	728	395
	(33.8%)	(39.4%)	38.8%	37.4%	42.9%	(33.5%)	(48.7%)	(34.8%)	(47.4%)	41.9%	(50.4%)	(48.0%)	(44.2%)
Fever	128	17	38	9	25	8	89	1	15	8	16	166	87
>38.5°C	(6.8%)	(7.7%)	5.9%	8.4%	(7.8%)	(4.6%)	(11.9%)	(2.2%)	(9.6%)	6.8%	(11.9%)	(10.9%)	(9.7%)
Arthralgia	279	36	96	17	51	20	161	5	37	15	29	314	160
	(14.7%)	(16.3%)	14.9%	15.9%	(15.8%)	(11.6%)	(21.6%)	(10.9%)	(23.7%)	12.8%	(21.3%)	(20.7%)	(17.9%)
Myalgia	452	57	166	32	106	51	254	16	53	30	55	501	284
	(23.9%)	(26.0%)	25.8%	29.9%	(32.9%)	(29.5%)	(34.1%)	(34.8%)	(33.9%)	25.6%	(40.7%)	(33%)	(31.8%)
Rash	278	38	57	18	48	22	139	3	34	23	31	321	169
	(14.7%)	(17.2%)	8.9%	16.8%	(14.9%)	(12.7%)	(18.7%)	(6.5%)	(21.8%)	19.7%	(23.0%)	(21.1%)	(18.9%)
Itching	229	23	64	7	45	21	101	5	26	16	18	194	113
	(12.1%)	(10.4%)	9.9%	6.5%	(14.0%)	(12.1%)	(13.6%)	(10.9%)	(16.7%)	13.7%	(13.3%)	(12.8%)	(12.6%)
Other	211	19	57	9	41	17	92	4	27	12	20	191	86
	(11.6%)	(8.6%)	8.9%	8.4%	(12.7%)	(9.8%)	(12.4%)	(8.7%)	(17.3%)	10.3%	(14.8%)	(12.6%)	(9.6%)
N=	1,892	221	644	107	322	173	745	46	156	117	135	1,518	894
BCRT	Source: Tomas Jelinek. Data on												

Dengue Vaccination in Travellers: Problems and Challenges

- Dengue is well known by many travellers,
- Reports of dengue outbreaks motivate travellers
- Image of dengue vaccine suffered from CYD-TDV
- Awareness of potential ADE risk in experts
- Public expert statements tend to be overcautious, ignoring the risk of infection
- Complaints by vaccinees after checking internet
- Enormous increase of mails and phone calls
- Vaccinees informed about SE of vaccination
- Last minute vaccination not advisable due to SE
- Vaccine is expensive,

BCRT

