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Acute Gastroenteritis Associated with Norovirus GII.8[P8], Thailand, 2023

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Acute gastroenteritis associated with human norovirus infection was reported in Phuket, Thailand, in June 2023. We amplified GII.8[P8] from the outbreak stool specimens. Retrospective sample analysis identified infrequent GII.8[P8] in the country beginning in 2018. In all, the 10 whole-genome GII.8[P8] sequences from Thailand we examined had no evidence of genotypic recombination.

Norovirus is the most common cause of acute viral gastroenteritis among adults and children and has no currently approved vaccine (*1*). Norovirus is genetically diverse and is classified into 10 genogroups (GI–GX) representing ≈50 genotypes, of which GI and GII predominantly infect humans (*2*). Currently, dual-typing of the RNA-dependent RNA polymerase (RdRp) gene in the open reading frame 1 region and the major capsid protein (VP1) gene in the open reading frame 2 region is required for proper genotype assignment and detection of viral recombinants (*3*).

In June 2023, health officials in Thailand were investigating diarrheal outbreaks that occurred on Phuket Island in southern Thailand, which is frequented by international travelers (https://www.bangkokpost.com/thailand/general/2592541/phukets-diarrhoea-outbreak-wanes-cause-still-unknown). Two stool specimens were eventually sent to our laboratory at the Center of Excellence in Clinical Virology at Chulalongkorn University (Bangkok) for molecular typing. The study was approved by Chulalongkorn University Institutional Review Board (approval no. 549/62). After viral RNA extraction from the stool specimens, quantitative real-time reverse transcription PCR (*4*) identified GII norovirus in both specimens. Confirmation assays using conventional reverse transcription PCR (*5*) with additional primers (Appendix 1 Table 1) and nucleotide sequencing yielded near-complete genomes, which we subjected to the norovirus genotyping tools of the Netherlands' National Institute for Public Health and the Environment (https://www.rivm.nl/mpf/norovirus/typingtool) and the US Centers for Disease Control and Prevention (https://calicivirustypingtool.cdc.gov).

Both specimens from Phuket were human norovirus GII.8[P8]. Because GII.8[P8] is relatively uncommon and rarely linked to large outbreaks, we retrospectively examined archived stool specimens dating back to 2018 to determine the frequency of past infection in the country. We identified 8 additional GII.8 strains (Table), all of which were GII.8[P8]. We deposited these complete genome sequences in GenBank (accession nos. OR546391–OR546400).

All 10 patients who tested positive for GII.8[P8] were relatively young (age range 3–29 years, mean age 10.8 years ± 7.1 SD). Five patients had vomiting and diarrhea, 3 had vomiting only, and 2 had diarrhea only (Appendix 1 Table 2, https://wwwnc.cdc.gov/EID/article/30/1/23-1264-App1.pdf). Minor symptoms were nausea, abdominal pain, fever, and headaches. All but 1 patient required 1–2 nights of hospital stay.

Table. Human norovirus GII.8[P8] strains identified in Thailand, 2018–2023

Collection date	Specimen ID	Patient age, y/Sex	Location	Specimen type
2018 Feb 2	B4899	5/M	Saraburi	Stool
2018 Feb 18	B5182	7/M	Bangkok	Stool
2018 Sep 18	B6213	6/F	Nonthaburi	Stool
2019 Jul 30	B6941	12/M	Nonthaburi	Stool
2020 Feb 04	B7634	29/F	Bangkok	Stool
2023 Feb 22	B9202	3/M	Bangkok	Stool
2023 Feb 27	B9256	12/F	Chaiyaphum	Stool
2023 Apr 19	B9804	10/M	Bangkok	Stool
2023 Jun 14	B10039	12/F	Phuket	Rectal swab
2023 Jun 13	B10069	7/F	Phuket	Stool

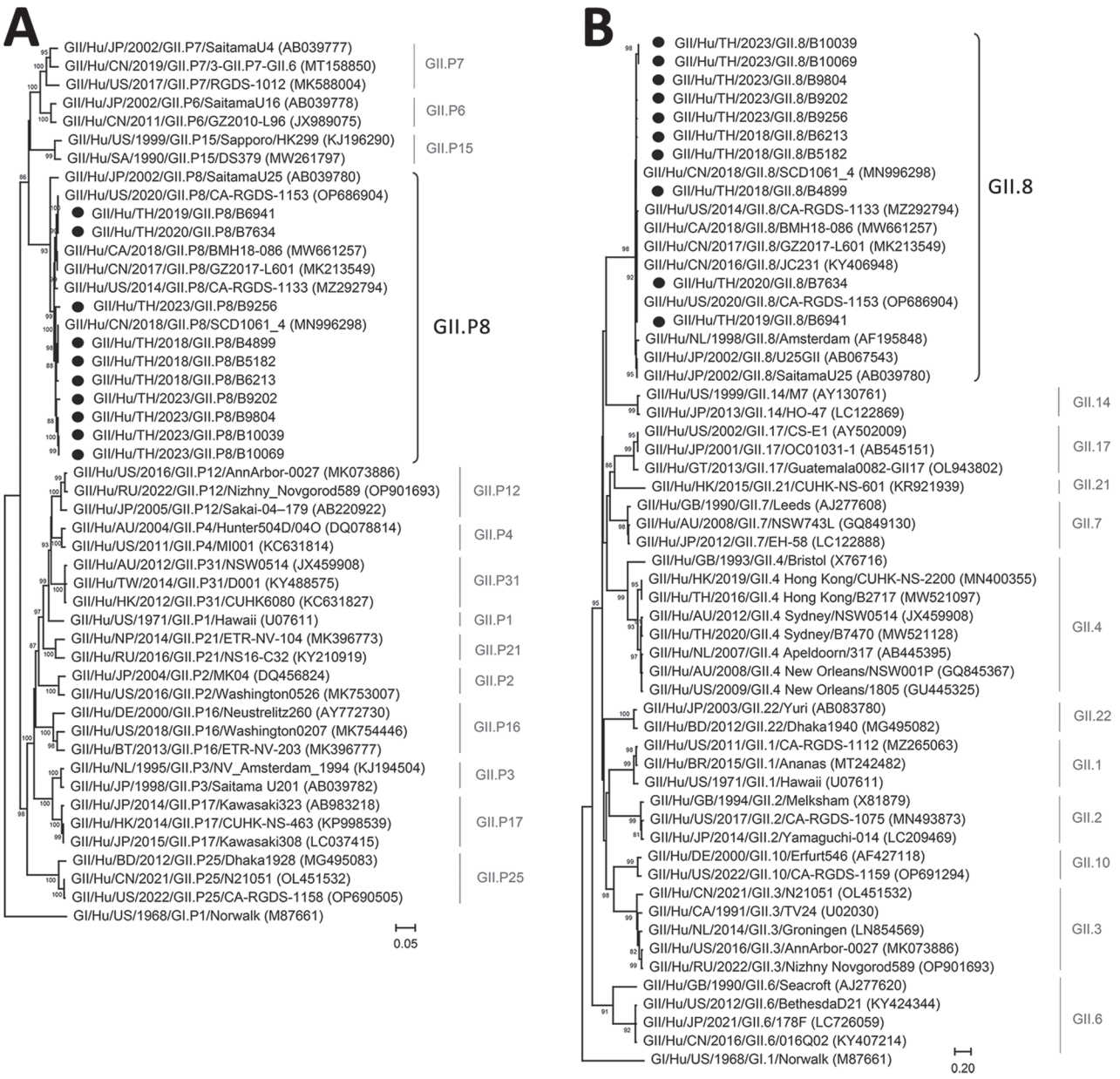

Figure. Phylogenetic analysis of the complete nucleotide sequences of noroviruses identified in Thailand, 2018–2023 (black dots), and reference sequences. A) RNA-dependent RNA polymerase (RdRp) region; B) major capsid protein (VP1) region. Trees were generated using the maximum-likelihood method based on the general time reversible model, with 1,000 bootstrap replications for branch support as implemented in MEGA software version 11 (http://www.megasoftware.net). Bootstrap values ≥80 are indicated at the branch nodes. GenBank accession numbers for reference sequences are provided in parentheses. Scale bar indicates nucleotide substitutions per site.

From the complete nucleotide sequences of the RdRp and VP1 genes, the GII.8[P8] strains from Thailand phylogenetically clustered with strains identified in Canada (GenBank accession no. MW661257), China (GenBank accession nos. MK213549 and MN996298), and the United States (GenBank accession nos. MZ292794 and OP686904) during the previous 10 years (Figure). Collectively, nucleotide sequence identities of GII.8[P8] strains from Thailand and other strains were 85%–99% over the entire genome compared with the prototypic GII.8[P8] SaitamaU25 (GenBank accession no. AB039780) (Appendix 1 Figure). However, Phuket GII.8[P8] appeared to diverge most from other GII.8[P8] strains in parts of the nonstructural protein 1–2 (p48), nonstructural protein 3 (NTPase), and VP1 shell domain.

To address whether Phuket GII.8[P8] strains had developed notable amino acid changes on its genome, we compared their deduced residues to other GII.8[P8] strains. Phuket GII.8[P8] shared many unique residue changes with the most recent strain from Thailand (B9804) identified in Bangkok 2 months prior (Appendix 2 Table, https://wwwnc.cdc.gov/EID/article/30/1/23-1264-App2.xlsx). No apparent mutations to suggest increased virulence or viral transmissibility were obvious, although ≥10 residue positions scattered throughout the GII.8[P8] genome identified in Thailand in 2023 were not shared by other known GII.8[P8] sequences. Most residue variations were conservative changes; however, T479S on VP1 is a highly conserved position among GII noroviruses.

The potential for GII.8[P8] to cause the recent norovirus outbreak in Phuket was unexpected given that the last reported outbreak in Thailand wad caused by a novel GII.3[P25] recombinant in Chanthaburi Province (*6*). Of note, GII.8[P8] outbreaks are infrequent (*7*), and the most recent occurrence was foodborne (through contaminated raspberries) (*8*). No specific food source was identified and laboratory-confirmed for norovirus, and anecdotal evidence suggests probable person-to-person norovirus transmission in the Phuket outbreak. Reports of GII.8[P8] infection in the literature have not identified RpRp–VP1 recombinants, and comprehensive historical analysis of norovirus sequences suggests that GII.8 RdRp and VP1 rarely recombine with other genotypes (*9*).

Molecular analysis in this study was limited because <40 complete GII.8[P8] genomes were available in the public database. This study was also constrained by the scarcity of specimens sent for laboratory testing, which underscored limited awareness and importance placed by health officials toward timely etiologic diagnosis. A study suggests that antibodies elicited by GI.1 and GII.4 (2 genotypes in the norovirus vaccine candidate under consideration) minimally block the binding of GII.8 VLPs to histo–blood group antigens (*10*). Although unlikely, any potential increase in the prevalence of GII.8[P8] could affect real-world norovirus vaccine effectiveness. In summary, GII.8[P8] genomes identified in this study are expected to contribute to the ongoing molecular and epidemiologic surveillance of community-acquired norovirus infection, which could benefit the tracking of global norovirus transmission.

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Use of Doxycycline to Prevent Sexually Transmitted Infections According to Provider Characteristics

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Use of doxycycline to prevent sexually transmitted infections (STIs) may lead to antimicrobial resistance. We analyzed attitudes toward this practice between US providers who commonly and less commonly treat STIs. Providers who more commonly treat STIs are more likely to prescribe prophylactic doxycycline and believe that benefits outweigh potential for increased antimicrobial resistance.

Reports of bacterial sexually transmitted infections (STIs) (e.g., chlamydia, gonorrhea, and syphilis) in the United States are at the highest level in several decades (*1*). A useful tool for preventing STIs may be prophylactic use of doxycycline taken within 72 hours after a sexual encounter (*2*–*5*). However, concerns about development of antimicrobial resistance (AMR) (e.g., in *Neisseria gonorrhea*, which is listed by the Centers for Disease Control and Prevention as an urgent AMR threat), may affect provider attitudes toward prophylactic use of doxycycline (*6*). To determine differences in the practices and beliefs of providers who work with STI patients (STI providers) and do not work with STI patients (non–STI providers) with regard to prophylactic use of doxycycline for STIs and their concerns about potential AMR consequences, we analyzed survey responses.

We analyzed data from the DocStyles panel survey (https://styles.porternovelli.com/docstyles) conducted by SERMO, a social network platform for physicians (https://www.sermo.com) in conjunction with Porter Novelli during September 9–November 3, 2022. Of 1,755 US healthcare providers who responded (response rate 67.0%), we focused on a sample of 1,504 healthcare providers, including family physicians (457, 30.4%), internists (545, 36.2%), obstetrician/gynecologists (251, 16.7%), and nurse practitioners/physician assistants (251, 16.7%). We excluded 251 pediatricians.

We further stratified analyses by the percentage of the providers' practice focused on clinical management of STIs. Providers were asked, "What proportion of your visits include screening for, diagnosing, or treating sexually transmitted infections?"; the 5 possible responses were "none," "some, but less than 10%," "more than 10% up to 25%," "more than 25% up to 50%," or "more than 50%." The 743 respondents whose practice consisted of <10% STI management were considered non–STI providers, and the 761 others were considered STI providers. We further ascertained provider age, sex, specialty, and number of years in practice.

We asked 4 questions about use and beliefs with regard to doxycycline prophylaxis and antimicrobial resistance (Figure), and the 5 response choices were "strongly disagree," "somewhat disagree," "neither agree nor disagree," "somewhat agree," or "strongly agree." We used χ^2 tests to compare the percentage of respondents who chose "strongly agree," and "agree" between STI providers and non–STI providers. We further tested those differences by using adjusted logistic regression models controlling for provider age, sex, number of years in practice, and specialty (Table).

Among STI providers, 41.9% said that they had ever prescribed doxycycline for STI prophylaxis, compared with 21.0% non–STI providers ($p<0.01$). Among STI providers, 57.4% either strongly agreed or agreed with the statement, "I have seen an increase in antibiotic resistant infections among my patients over the past 5 years," compared with 57.6% of non–STI providers ($p = 0.94$). Among STI providers, 63.5% either strongly agreed or agreed with the statement,

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Appendix 1

Appendix 1 Table 1. Primers used to amplify the complete genomes of norovirus GII.8[P8]

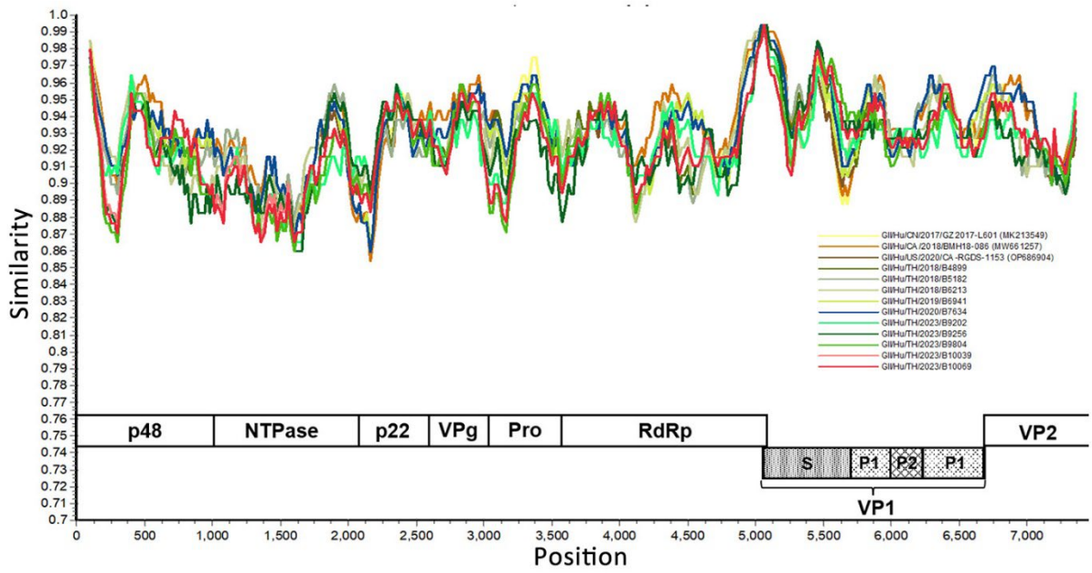
ORF	Primer name	Sense	Sequence (5′-3′)	Position*
1	F1_GII.P8_1	F	GTGAATGAAGATGGCGTCTAAC	1–22
	1R_GII.P8_1180	R	CATGACCAATTTAAGTATGTCAAGG	1156–1180
	F2_GII.P8_968	F	TCGAACTTCATCGCGTCAC	968–986
	2R_GII.P8_2028	R	ATAGTCCCCTTCCCATGTGG	2009–2028
	F3_GII.P8_1913	F	CAACCAGACATGTGGAAGG	1913–1931
	3R_GII.P8_2924	R	CTGTGACGAGTCCCAGAAC	2906–2924
	F4_GII.P8_2752	F	CACAATAGAGGAGTACCTCCA	2752–2772
	4R_GII.P8_3912	R	TCCAATGAAGCACAGGCTT	3894–3912
	F5_GII.P8_3743	F	TCACTCCAACAAGTGATGC	3743–3761
	5R_GII.P8_4699	R	CTCAGTTTTGTCTGGCCTT	4681–4699
	RdRpF1_GII.P8_3380	F	ATGGGCATGCTGCTCACTG	3380–3398
	RdRp1R_GII.P8_4317	R	GTTGAGTCCCACCTAGAGTA	4298–4317
	RdRpF2_GII.P8_4049	F	ATGTACACAGCAGCCCTCAA	4049–4068
	RdRp2R_GII.P8_5165	R	CATGACCTCATGGTTGATCTC	5145–5165
2	F1VP1_GII.8_4967	F	ATCAAGAGTGGTGGTCTGGA	4967–4986
	1RVP1_GII.8_5659	R	CCAGCATTGTTAGCCCTTAGG	5639–5659
	F2VP1_GII.8_5403	F	ATAGTGCTTGCTGGGAATG	5403–5421
	2RVP1_GII.8_6393	R	CTGGCATGAACGAGCGGAA	6375–6393
	F3VP1_GII.8_6128	F	ACATGAGGCTAGGGTCAAC	6128–6146
	3RVP1_GII.8_6980	R	TGGTTGGAGCATTGATGGAAC	6960–6980
	F4VP1_GII.8_5786	F	ATCTGAGATGACAAATTCAAGAT	5786–5808
	F5VP1_GII.8_6127	F	CACATGAGGCTAGGGTCAA	6109–6127
3	VP2F1_GII.8_6616	F	ACTTCAGGTTTGAGGCATGG	6616–6635
	VP2R1_GII.8_7484	R	TCATTCTTTTCACTAAGCCCGTG	7462–7484
	VP2R2_GII.8_7497	R	ATAATCTAACCAAATCATTCTTTTCACTA	7469–7497

*Based on GII/Hu/JP/2002/GII.P8/SaitamaU25 (GenBank accession number AB039780).

Appendix 1 Table 2. Detailed clinical characteristics of individuals who tested positive for norovirus GII.8[P8]*

	Sample ID									
Parameter	B4899	B5182	B6213	B6941	B7634	B9202	B9256	B9804	B10039	B10069
Age (years)	5	7	6	12	29	3	12	10	12	7
Gender	Male	Male	Female	Male	Female	Male	Female	Male	Female	Female
Location	Saraburi	Bangkok	Nonthaburi	Nonthaburi	Bangkok	Bangkok	Chaiyaphum	Bangkok	Phuket	Phuket
Collection date	2018 Feb 02	2018 Feb 18	2018 Sep 18	2019 Jul 30	2020 Feb 04	2023 Feb 22	2023 Feb 27	2023 Apr 19	2023 Jun 14	2023 Jun 13
Setting	Hospitalized	Hospitalized	Hospitalized	Hospitalized	Hospitalized	Hospitalized	Outpatient	Hospitalized	Hospitalized	Hospitalized
Hospital stay (nights)	2	1	2	1	2	1	0	1	2	2
Diarrhea duration (days)	1	1	1	1	1	No	NI	1	3	No
Symptoms								Symptoms		
Diarrhea (per day)	5–6 times	NI	NI	2 times	1 time	No	No	NI	10 times	No
Vomiting (per day)	5–6 times	>10 times	3 times	No	No	3 times	5 times	5 times	5 times	>10 times
Nausea	No	No	No	No	Yes	No	Yes	Yes	NI	Yes
Abdominal pain	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes
Fever	No	Yes	No	No	No	No	No	No	Yes	No
Headache	No	No	No	No	Yes	No	Yes	No	NI	NI
Vital signs								Vital signs		
Body Temperature (°C)	37	38.7	36.9	36.5	36.9	36.5	36.9	37.4	38	37.2
Pulse rate (per min.)	140	124	120	108	90	136	73	116	122	148
Respiratory rate (per min.)	20	20	22	20	20	22	18	20	24	24
Blood pressure (mmHg)	121/64	114/77	101/63	126/70	99/54	112/64	107/60	103/54	99/57	94/63
Serum leukocyte (cells/mm^3)	17,800	15,140	12,050	12,920	7,520	24,490	NI	15,350	10,160	13,310
Mode of transmission	NI	NI	NI	NI	NI	NI	NI	NI	Person-to-Person	Person-to-Person

*NI, no information.



Appendix 1 Figure. Nucleotide sequence similarities among the ten GII.8[P8] Thai strains and three selected reference strains (GenBank accession numbers MK213549, MW661257, and OP686904) compared to the Norovirus Classification Working Group prototype GII/Hu/JP/2002/GII.P8/SaitamaU25 (AB039780) as query. Analysis was performed using SimPlot program version 3.5.1.