Controlling Norovirus Transmission in Retail and Food Service: How Possible is Possible?

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NoroCORE Food Virology
Collaborative for Outreach, Research & Education

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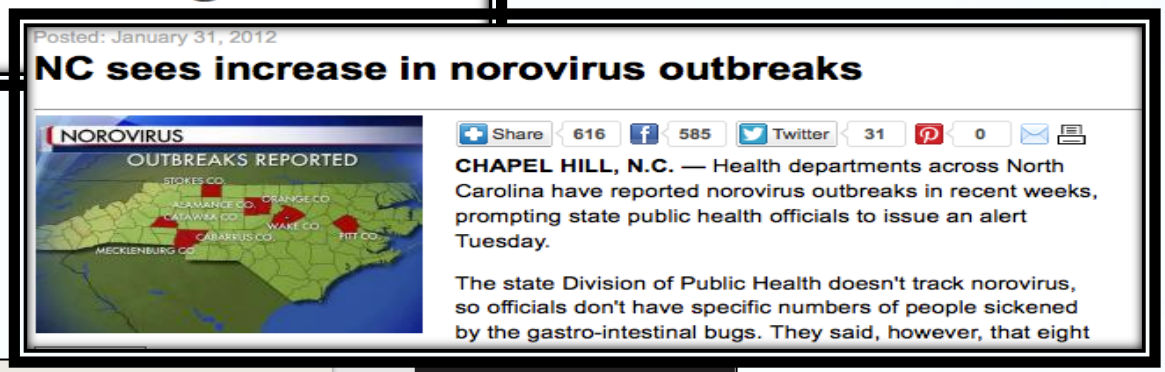
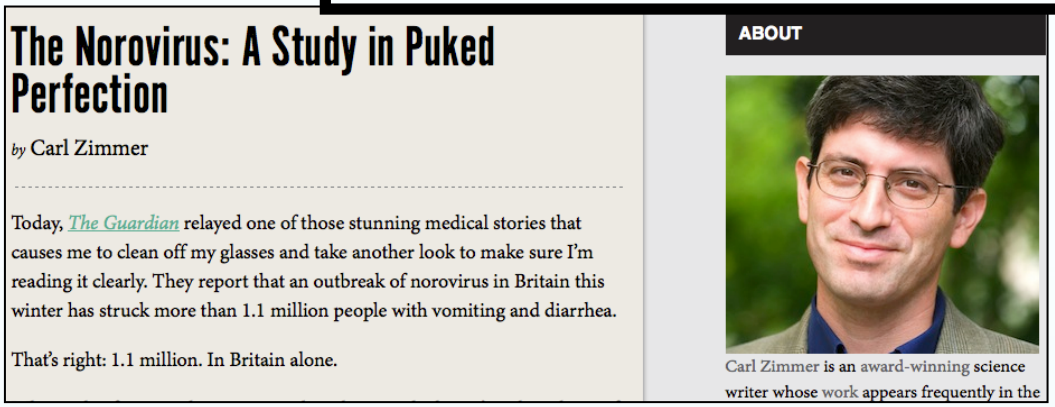
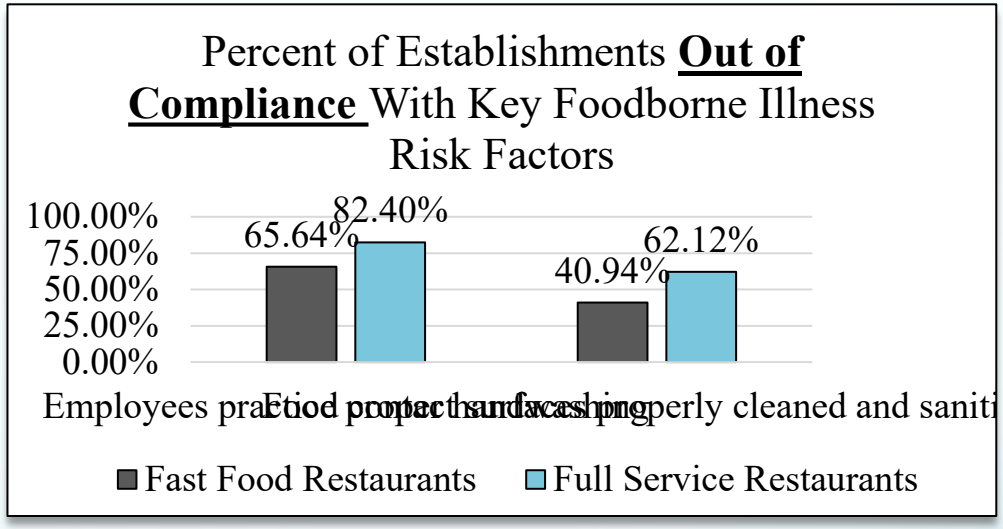




- Fecal-oral transmission
- Humans only
- "Within a day of infection, noroviruses have rewired our digestive system so that **<u>stuff comes flying out from both ends</u>**" – Carl Zimmer in a recent National Geographic article.
  - Vomiting, watery diarrhea, nausea, and abdominal pain.
  - Usually self limiting, but in some instances (individuals with weak immune systems), complications from dehydration can develop.

Controlling Foodborne Illness Outbreaks at Retail

- The CDC identifies 5 major risk factors contributing to foodborne illness outbreaks:
  1. Poor personal hygiene
  2. Food from unsafe sources
  3. Improper cooking
  4. Improper holding (time/temperature)
  5. Contaminated equipment



Most recent (2013-2014) results from FDA's 10-year risk factor study, representing 425 Fast Food Restaurants and 396 Full-Service Restaurants. Available at https://www.fda.gov/media/117509/download

Epidemiological Significance

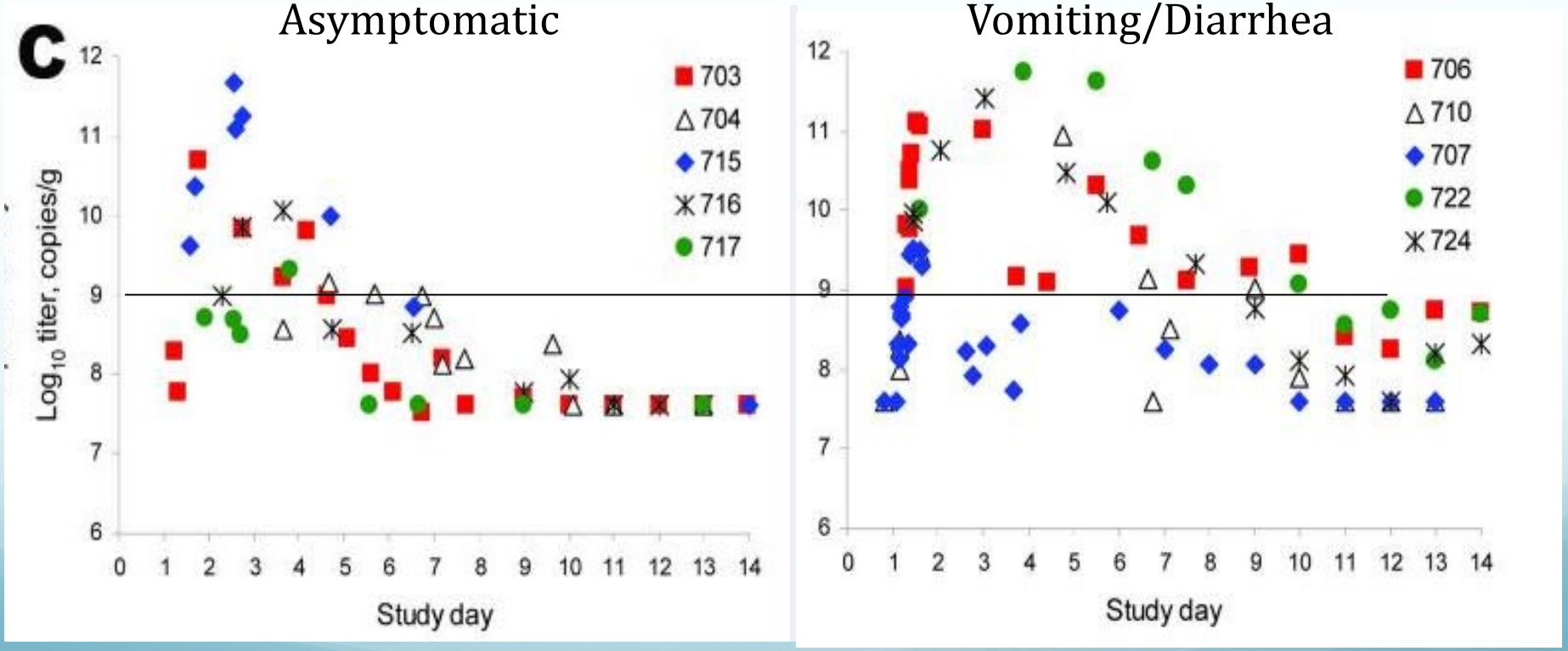
- Human norovirus (hNoV) responsible for ~20-25% of gastroenteritis worldwide
- Modes of transmission
  - Predominantly person-to-person (~20 million annual total U.S.)
  - 20-25% of cases foodborne (5+ million annual total U.S.))
- Leading cause of foodborne illness in the U.S.
  - Infected food handlers cause about 70% of reported norovirus outbreaks from contaminated food (when a cause is found)
  - In over half of these cases the workers had barehand contact with ready-to-eat foods (Hall et al., 2014)
- Based on analysis of CDC NORS data (Hall et. al., 2012)
  - 64% Restaurants
  - 17% Catering/banquet facilities
  - 13% Other

Virus Features Impacting Risk and Control Strategies

Low infectious dose
Copious shedding in feces of infected individuals
Role of vomiting
Ease of contamination of surfaces and hands
Environmental persistence

Human Norovirus Infectivity and Shedding

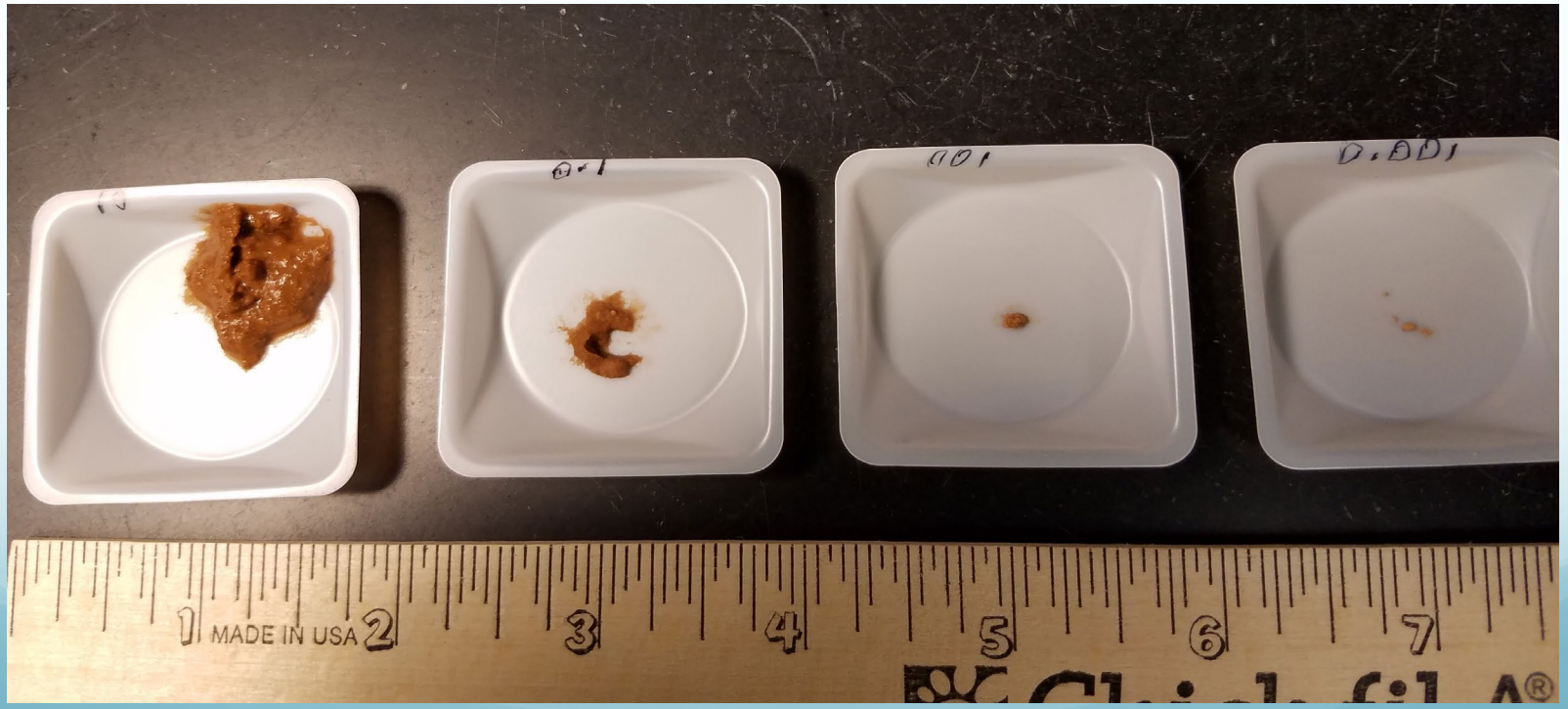
- Low infectious dose (≥18 viral particles; closer to 100-1,000?)
- Copious shedding (10^5–10^{11} viral copies per gram of feces), even among asymptomatic infections
- Lower degrees of shedding post-symptomatically, but extended
- **Justification for exclusion of ill food workers**



Atmar et al. 2008. Emerg Infect Dis.14(10):1553-7.

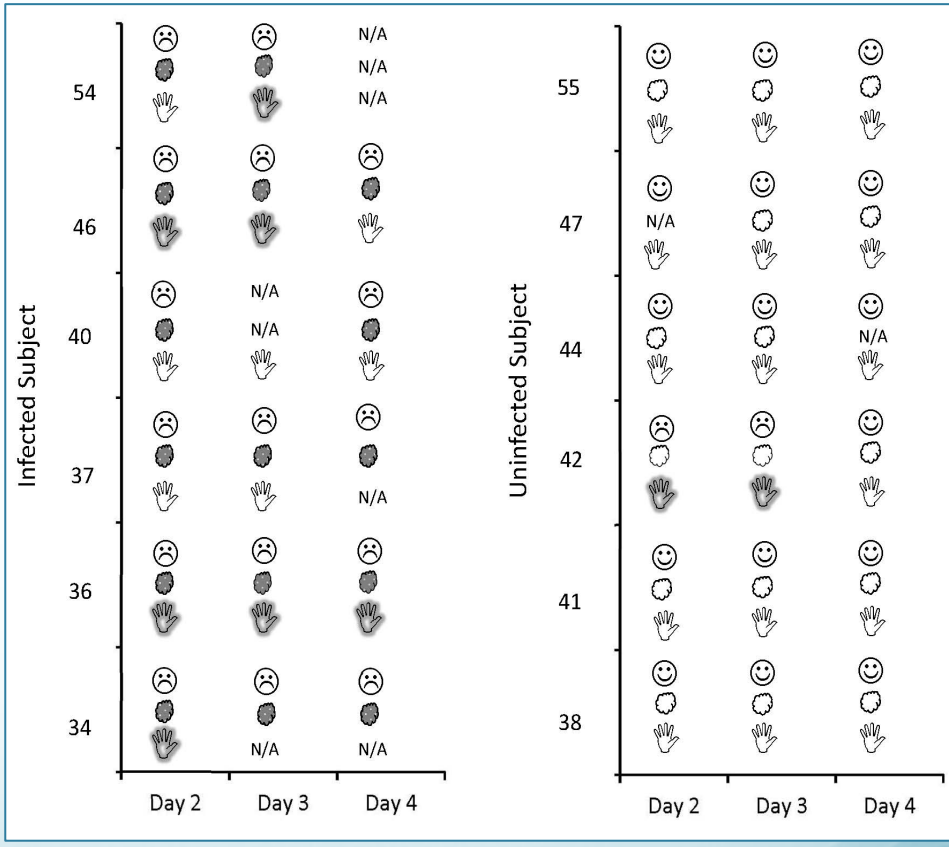
Estimated Virus Concentrations

hNoV conc':	1-100 million (M)	100,000-10 M	10,000-1 M	1,000-100,000
Fecal inoculum:	1 g	1/10th g	1/100th g	1/1,000th g



Contamination of Hands

- Hand carriage in experimentally-infected individuals (Liu et al., 2013)
  - While more common with those with symptoms, there was a case of hand contamination in an uninfected person who had been in the room of someone who was infected.
- **Justification for hand hygiene and no bare contact with RTE foods**



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RESEARCH ARTICLE

Vomiting as a Symptom and Transmission Risk in Norovirus Illness: Evidence from Human Challenge Studies

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PLOS ONE

Table 3. Norovirus Titers in Emesis.

Study	# Subjects with Emesis Specimens	# Emesis Specimens	% Subjects with ≥ 1 Positive Emesis	% Positive Samples	Sample Mean Titer[c] (GEC[d]/ml)(SEM[e])	Subject Mean Cumulative Shed (GEC[d])(SEM[e])
1	6	16	50%	63%	$5.8x10^5$ ($2.6x10^5$)	$1.3x10^8$ ($9.1x10^7$)
2	8	20	75%	90%	$9.2x10^5$ ($3.1x10^5$)	$3.1x10^8$ ($1.7x10^8$)
All GI	14	36	64%	78%	$8.0x10^5$ ($2.2x10^5$)	$2.3x10^8$ ($1.0x10^8$)
3	4[a]	8	25%	38%	$1.6x10^5$ ($4.5x10^4$)	$1.8x10^7$ ($1.8x10^7$)
4	2	13	100%	92%	$5.0x10^3$ ($2.7x10^3$)	$2.3x10^5$ (ND)[b]

Justification for vomit and fecal material clean-up guidelines

Environmental Persistence-- Experimental

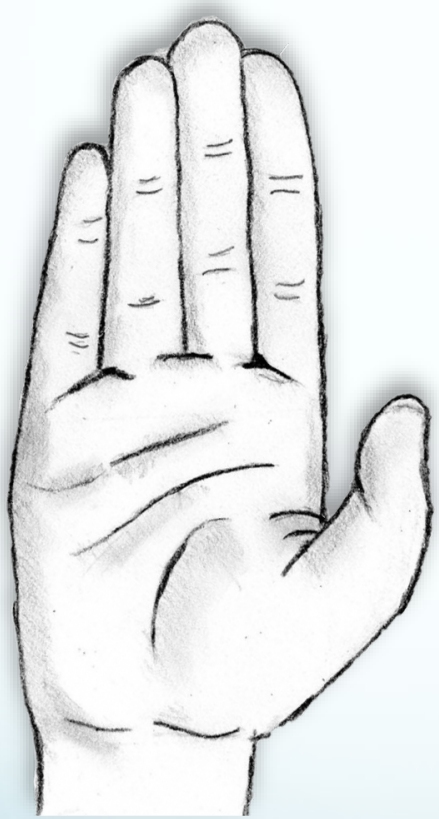
TABLE 3. *Survival of norovirus on various fomites and material surfaces*[a]

Surface	Temp (°C)	RH (%)	NoV genogroup	Time to first log decrease in GE (days)	Approx overall log decline of GE	Reference
Ceramic	22	NG	I	ND	3 in 28 days	49
	22	NG	II	ND	0.4 in 42 days	49
	25	NG	I	ND	1 in 50 h[b]	71
	RT	NG	I	34[c]	1.5 in 42 days[b]	20
	NG	NG	II	ND	1.2 in 42 days	52
	RT	NG	II	33[c]	<1 in 42 days[b]	20
Formica	22	NG	I	ND	1.6 in 28 days	49
	22	NG	II	ND	0.6 in 42 days	49
	NG	NG	II	ND	0.8 in 42 days	52
	RT	NG	I	29[c]	1.5 in 42 days[b]	20
	RT	NG	II	33[c]	1.5 in 42 days[b]	20
PVC	7	86	II	ND	<1 in 56 days	42
	20	30	II	ND	2 in 14 days	42
	20	86	II	ND	2 in 35 days	42
Stainless steel	4	NG	I	>28[c]	0.9 in 4 wk	50
	7	86	II	ND	2 in 56 days	42
	7	50	II	>70	<1 in 70 days	60
	20	30	II	ND	2 in 14 days	42
	20	86	II	ND	2 in 35 days	42
	22	NG	I	ND	1.5 in 28 days	49
	22	NG	II	ND	0.5 in 42 days	49
	25	NG	I	ND	1 in 50 h[b]	71
	RT	NG	I	34[c]	1.5 in 42 days[b]	20
	RT	NG	I	21	1.5 in 28 days	50
	RT	NG	II	43[c]	<1 in 42 days[b]	20
	RT	50	II	30[c]	3 in 70 days	60
	NG	NG	II	ND	1.1 in 42 days	52
	37	NG	I	7	2.4 in 28 days	50

[a] RH, relative humidity; GE, genome equivalents; NG, not given; ND, not determined; RT, room temperature; PVC, polyvinyl chloride.
[b] Values estimated from graphical display of data.
[c] T90 values.

From: Cook et al. 2016. *J. Food Prot.* 79:1273-1294

Pathogen Survival on Skin

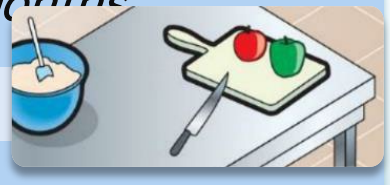


Pathogen	Duration of Persistence
Norovirus	**2 hours or more**
Hepatitis A	**5.5 to 7.7 hours**
Influenza A	*1/2 hour to 1 hour*
Escherichia coli	**Up to 1 ½ hour**
Klebsiella pneumoniae	**Up to 1 ½ hour**
Shigella	**Up to 3 hours**
Serratia marcescens	**Up to 1 ½ hour**
Staphylococcus aureus	**Up to1 ½ hour**

From: Kramer A. BMC Infectious Diseases 2006;6:130

Pathogen Survival on Surfaces

Type of Pathogen	Duration of Persistence
Escherichia coli	*1.5 hours - 16 months*
Norovirus	*4 - 6 weeks*
Hepatitis A	*3 weeks*
Listeria spp.	*1 day - months*
Salmonella typhi	*6 hours - 4 weeks*
Staphylococus aureus, incl. MRSA	*7 days - 7 months*
Shigella	*2 - 28 days*
Campylobacter	*1- 4 hours*

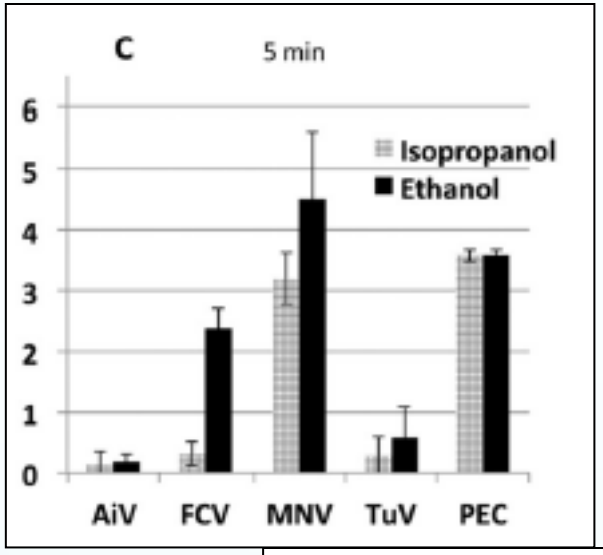


From: Kramer A. BMC Infectious Diseases 2006;6:130

Human Norovirus Persistence

- Surfaces
  - Room temperature: Days/ weeks
- Foods and water
  - Refrigeration: Weeks/months/ years
  - Freezing: Months/ years
- Also depends on surface/food and virus, RH
- Transferability
  - Variable (0.1%->90%)
  - Depends on moisture, surfaces, pressure, virus
  - Sequential (10X)
- Environmental contamination
  - *Outbreaks*
  - *Endemic*
  - *Virus concentrations*
  - *Relative importance of hands, surface, air to foodborne transmission (attribution)?*

The Conundrum: Reliability of Cultivable Surrogates



--Human norovirus is non-cultivable
--Regulatory considerations
--What do the data show?
--Ethanol, pH, chlorine
--Can one use molecular methods and HuNoV in place of the surrogates?

TABLE 1 Chlorine treatment of surrogate viruses dried on stainless steel discs

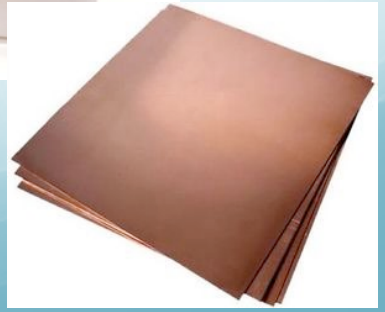
Chlorine concn (ppm)	Log_{10} reduction in infectivity[a] for:				
	AiV	FCV	MNV	PEC	TuV
200	0.9 ± 0.2	0.2 ± 0.7	0.1 ± 0.7	0.4 ± 0.1	0.3 ± 0.1
1,000	1.3 ± 0.9	5.3 ± 0.7	1.4 ± 0.4	1.2 ± 0.5	1.2 ± 0.2

[a] Values are means for 4 or more replicates from 2 separate experiments ± standard deviations.

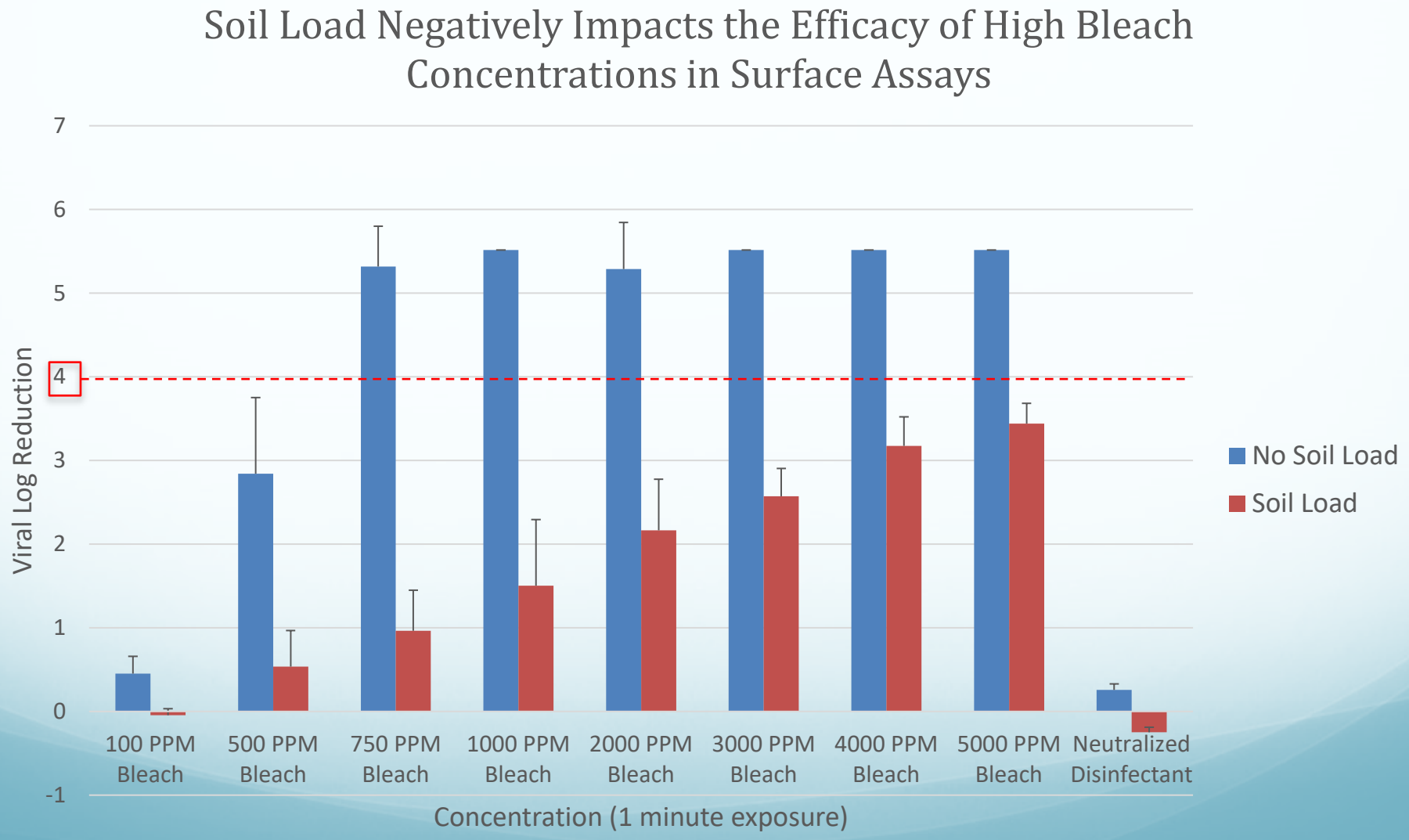
From: Cromeans et al., *App. Environ. Microbiol,* 2014.

Surface Sanitizing and Disinfection

- Formulation matters
- Application approach is important
- Label claim issues
- Efficacy impacted by concentration, contact time, soil
- Actives (ingredients)
  - Chlorine, 1,000-5,000 ppm (+)
  - Benzalkonium chloride chloride (-)
  - Phenols (-)
- Other products
  - *Hypochlorous acid, up to 250 ppm*
  - *Silver dihydrogen citrate*
  - *Activated hydrogen peroxide*
- Soft surfaces?



Bleach Surface Assays



Journal of
Applied Microbiology

ORIGINAL ARTICLE

Efficacy of a disinfectant containing silver dihydrogen citrate against GI.6 and GII.4 human norovirus

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Department of Food, Bioprocessing, and Nutrition Sciences, North Carolina State University, Raleigh, NC, USA

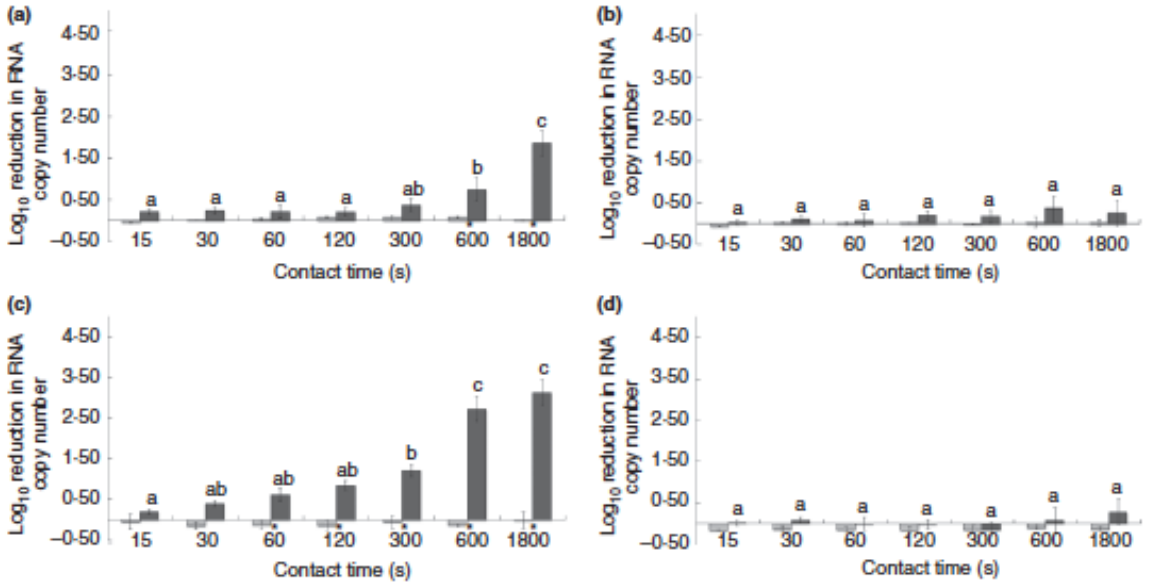
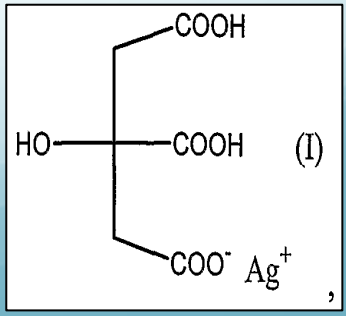
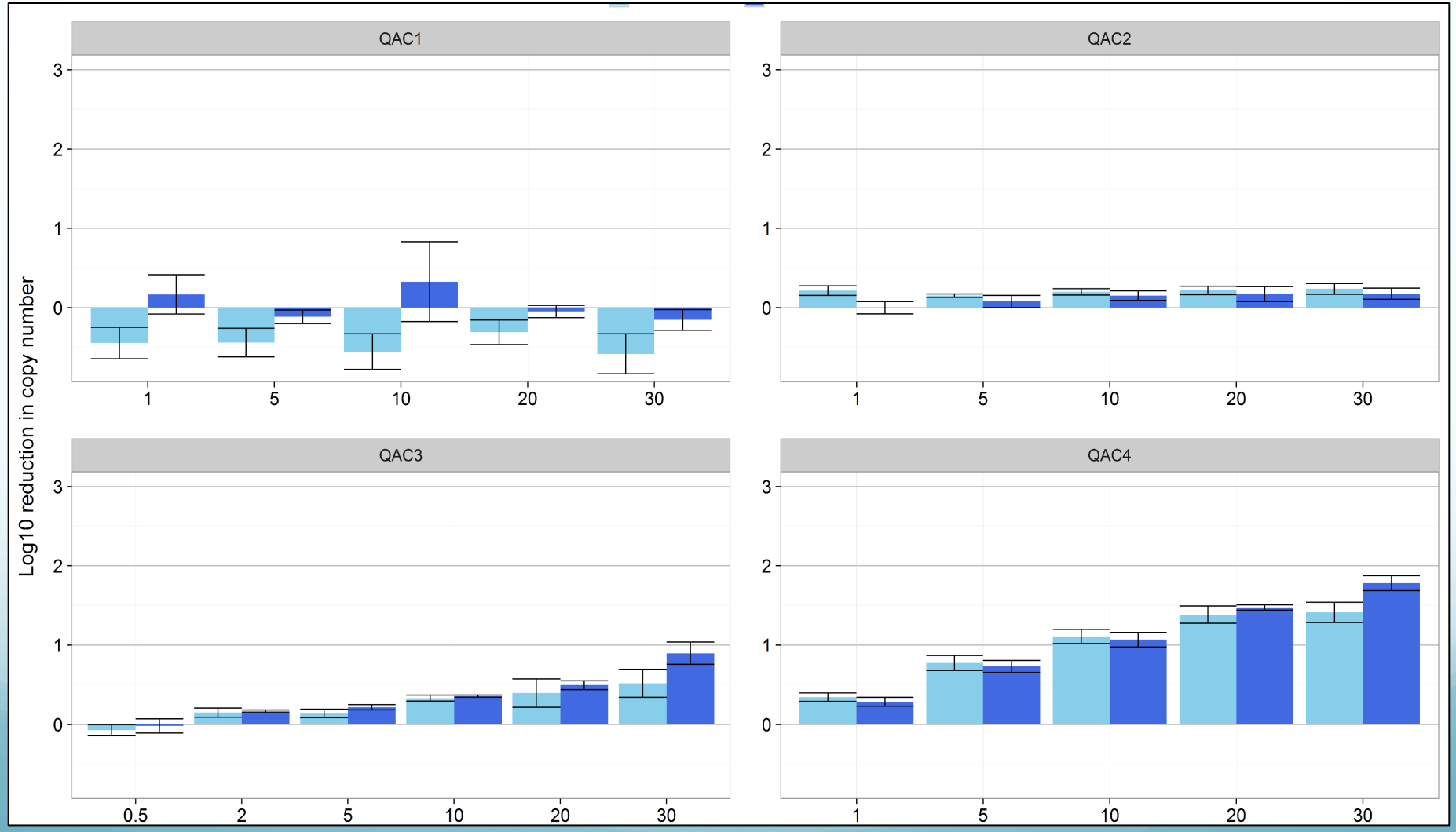


Figure 2 Effects of silver dihydrogen citrate (SDC) against GI.6 and GII.4 human norovirus samples dried onto stainless steel surfaces. Inactivation of human norovirus GI.6 (panels a and b) and GII.4 (panels c and d) by SDC as evaluated by RT-qPCR using carrier test. Clarified 20% faecal suspensions positive for either GI.6 or GII.4 human norovirus were placed onto sterile stainless steel carriers, allowed to dry and exposed to SDC-containing disinfectant, with (b and d) and without (a and c) additional soil load for 15 s to 30 min, followed by neutralization. The samples were extracted for RNA and analysed by RT-qPCR with an RNase pretreatment (■) and without an RNase pretreatment (□). Human norovirus RNA copy number was estimated by extrapolation to a standard curve. Letters above bars indicate statistically significant differences ($P < 0·05$) between time points for samples pretreated with RNase prior to RT-qPCR. Asterisks under bars indicate instances where statistically significant differences ($P < 0·05$) were observed between samples with and without RNase pretreatment. Error bars represent standard error of the mean. All experiments were performed in triplicate.



Quaternary Ammonium Compounds (QAC) Efficacy Summary



Journal of Applied Microbiology

How to cite this article: Escudero-Abarca, BI, Goulter, RM, Bradshaw, J, Faircloth, J, Leslie, RA, Manuel, CS et al. (2022) Efficacy of an alcohol-based surface disinfectant formulation against human norovirus. *Journal of Applied Microbiology*. 00:1–11. https://doi.org/10.1111/jam.15479

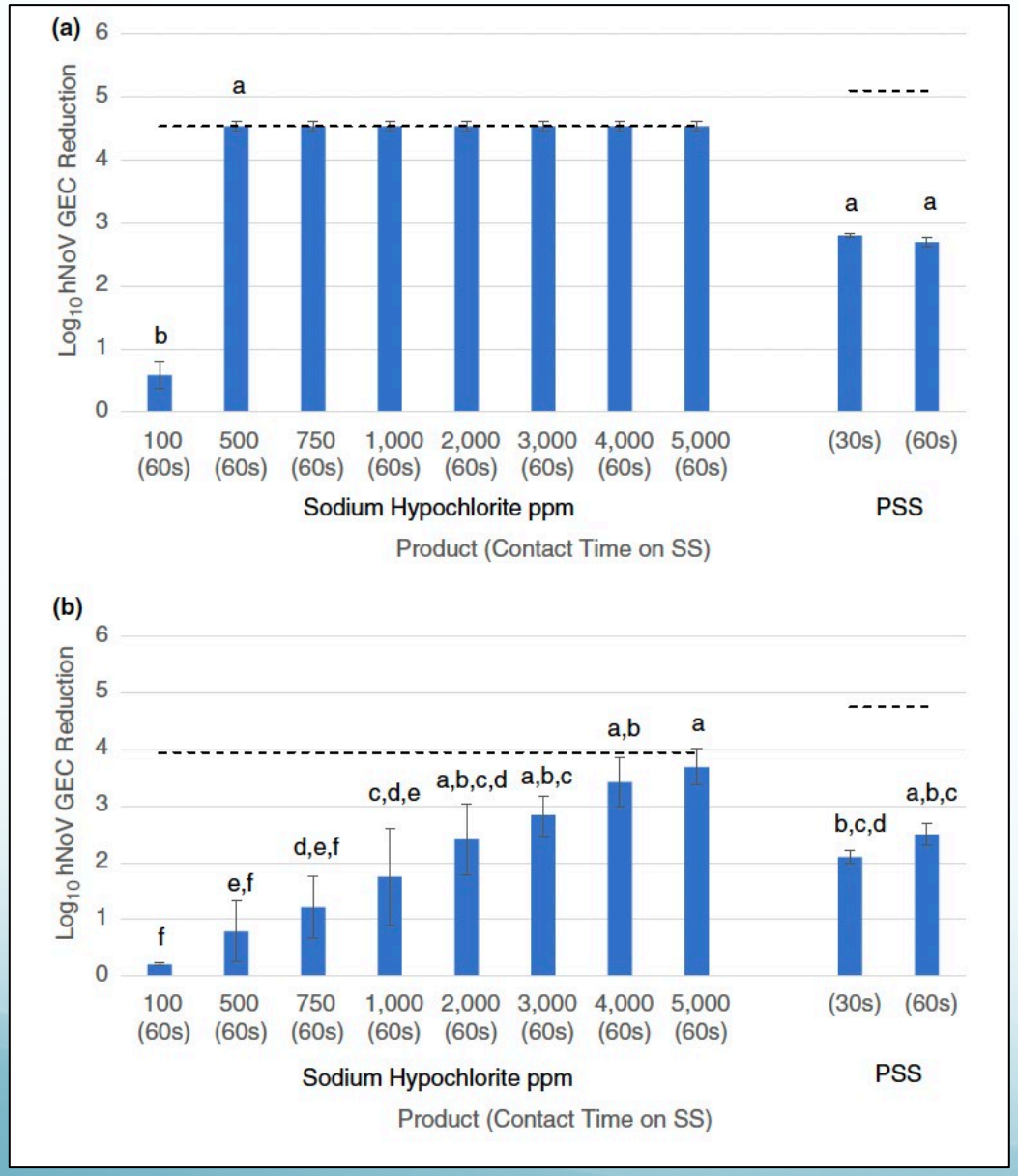


FIGURE 2 Efficacy of various sodium hypochlorite (60 s contact time) solutions and a commercially available alcohol-based surface sanitizer (PSS; 30 and 60 s contact times) against hNoV ($\log_{10}$ hNoV GEC reduction ± standard deviation as evaluated by RNase-RT-qPCR) on stainless steel (SS) surfaces (ASTM E1053-11) without additional soil added to the inoculum (Panel A; native soil load of ~2.5%) and with additional soil added to the inoculum (Panel B; total soil load of ~5%). The dotted lines represent the limit of detection (LOD) of the assays (LOD 3.9 and 4.7 $\log_{10}$ hNoV GEC for sodium hypochlorite and PSS assays, respectively). Different letters indicate statistically significant differences between treatment types (treatments reaching assay LOD were not included in the statistical analysis)

Characterizing Microbial Cross-Contamination on Large Surfaces Using a Traditional "Cloth and Bucket" Disinfection Method

Rebecca M. Goulter,[1*] James S. Clayton,[2] Robin Grant Moore,[1] Justin M. Bradshaw,[1a] Jason W. Frye,[1] Esa J. Puntch[1] and Lee-Ann Jaykus[1]

Food Protection Trends, Vol 40, No. 6, p. 392–401

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TABLE 1. Cross-contamination efficiency ratios of microorganisms from an inoculated laminate surface to a clean laminate surface with a single wiping step using the cloth and bucket method

Organism	Treatment	CFU/PFU on surface 1–dirty (mean ± standard deviation)	CFU/PFU on surface 1–clean (mean ± standard deviation)	Cross-contamination efficiency (mean ± standard deviation)[a]
L. innocua	PBS	7.24 ± 0.99	6.79 ± 0.88	1.08 ± 0.06
	QAC	3.77 ± 0.27	LOE[b]	N/A[b]
	QAC + 5% soil	4.18 ± 0.29	3.51 ± 0.38	1.20 ± 0.05
E. coli	PBS	5.26 ± 1.26	5.08 ± 1.29	1.05 ± 0.05
	QAC	3.19 ± 0.42	LOE[b]	N/A[b]
	QAC + 5% soil	3.72 ± 0.30	3.01 ± 0.40	1.28 ± 0.17
B. cereus	PBS	8.85 ± 0.06	8.75 ± 0.08	1.01 ± 0.01
	QAC	9.04 ± 0.34	8.90 ± 0.22	1.01 ± 0.02
	QAC + 5% soil	9.13 ± 0.16	9.20 ± 0.07	0.99 ± 0.02
MS2	PBS	6.34 ± 0.96	5.80 ± 0.86	1.09 ± 0.03
	QAC	5.51 ± 0.94	4.41 ± 0.78	1.26 ± 0.17
	QAC + 5% soil	5.50 ± 0.88	4.76 ± 0.22	1.15 ± 0.18

[a]Cross-contamination efficiency was calculated as a ratio of the total number of organisms on the inoculated side of S1d to the total number of organisms on S1c after the first wiping event (S1d/S1c).

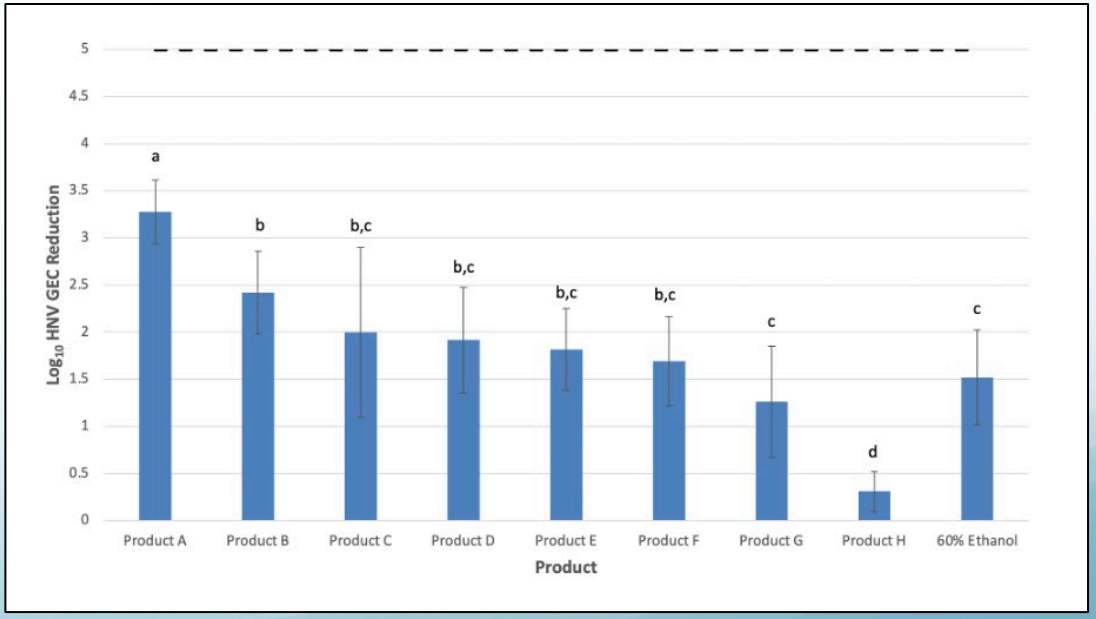
[b]Not applicable (N/A), when the organism was completely inactivated by the disinfectant (limit of enumeration [LOE] reached) and ratios could not be determined.

What We Don't Know

- Effect of wiping on:
  - Disinfection efficacy
  - Removal vs. "killing" vs. spreading
  - Cross-contamination
- Variables impacting wiping efficacy
  - Cloth type/Disinfectant type
  - Surface type
  - "Wetness"
  - Pressure
  - Time
  - Soil

A Word About Hand Sanitizers

- Formulation matters
- Product type [actives]
  - Alcohol [70-90%, ethanol, isopropanol, n-propanol] (+/-)
  - Benzalkonium chloride chloride (-)
  - Triclosan (-)
  - *Povidone-iodine (+/-)*
- Product application (volume and time)
- Validation issues
- Regulatory-licensing-use issues



Novel Technologies

What are they?
How do we know they work?
Where should they be used?
Validation

Where is Residual Contamination?

Prevalence of Human Noroviruses in Commercial Food Establishment Bathrooms

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Journal of Food Protection, Vol. 81, No. 5, 2018, Pages 719–728
doi:10.4315/0362-028X.JFP-17-419

TABLE 2. *Number of samples collected by state and number of samples positive for human norovirus as determined by real-time RT-PCR*

State	Sites visited	Bathrooms sampled	Surfaces sampled	No. of presumptive-positive samples[a]			% positive[b]
				GI	GII	Total	
New Jersey	286	377	1,505	14	13	27	1.8
Ohio	345	496	1,977	11	7	18	0.9
South Carolina	120	171	681	4	12	16	2.3
Total	751	1,044	4,163	29	32	61	1.5

[a] Number of swab samples that were positive after analysis. GI, genogroup I noroviruses; GII, genogroup II noroviruses.
[b] Number of positive swabs divided by the total number of swabs collected.

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0099-2240/11/$12.00 doi:10.1128/AEM.02354-10

Year-Round Prevalence of Norovirus in the Environment of Catering Companies without a Recently Reported Outbreak of Gastroenteritis[▽]

Ingeborg L. A. Boxman,[1]* Linda Verhoef,[2] Remco Dijkman,[1]† Geke Hägele,[1] Nathalie A. J. M. te Loeke,[1] and Marion Koopmans[2]

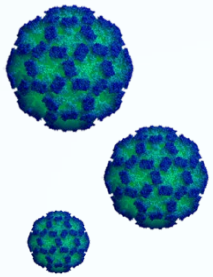
TABLE 1. Detection of NoV in environmental samples from catering companies with and without association with recently reported gastroenteritis

Parameter	Value where NoV detected in samples from:					
	Kitchen		Bathroom		All	
	No./total	%	No./total	%	No./total	%
Prevalence study (not related to outbreaks)						
Companies (total)	13/832	1.6	26/832	3.1	35/832	4.2
Samples	9/832[a]	1.1	26/832	3.1	42/2,496	1.7
	7/832[b]	0.84				
Total	16/1,664	0.96	26/832	3.1	42/2,496	1.7
Outbreak investigations (2006–2008)						
Companies						
2006	7/23	30	11/14	79	14/27	52
2007	11/20	55	10/16	63	14/22	63
2008	7/20	35	12/19	63	16/23	69
Total	25/63	40	33/49	67	44/72[c]	61
Samples						
2006	19/69	28	14/22	64	48/119	40
2007	22/72	30	17/33	52	51/121	42
2008	18/60	30	23/47	49	48/130	37
Total	59/201	29	54/102	53	147/370[c]	40

[a] Grips of refrigerator, mixing or cutting machines, and grip of bread knife.
[b] Salt-and-pepper set and soap dispenser.
[c] During outbreak investigations, samples from other locations outside the kitchen and the bathroom were also collected, e.g., handrails, telephones, and door handles in restaurants.

Novel Technologies: Examples

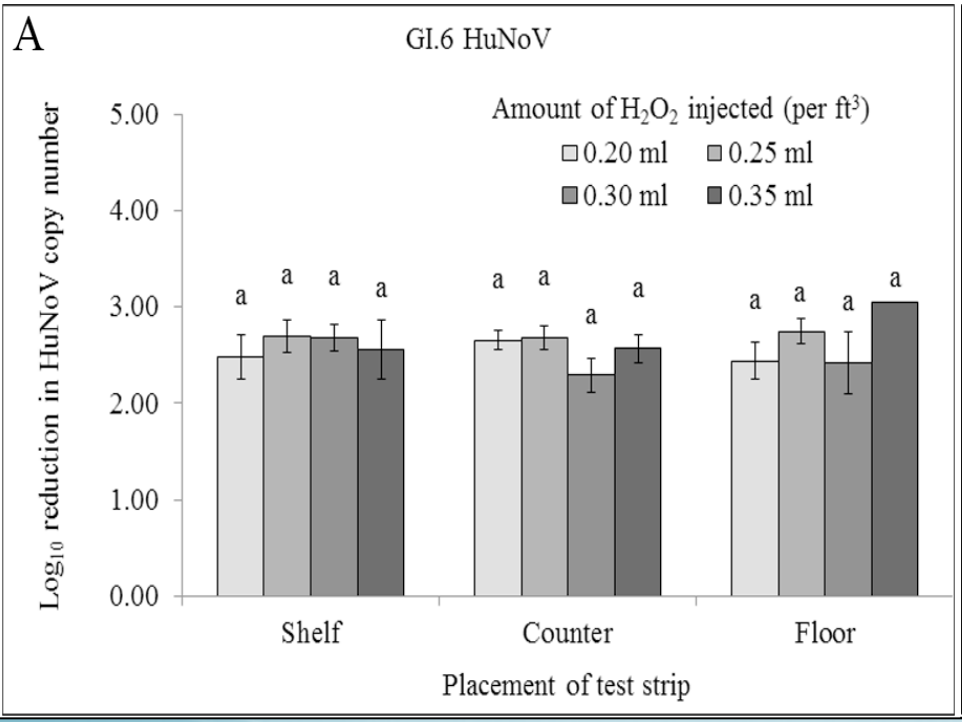
- Novel sanitizer and disinfectant formulations
- Antimicrobial surfaces (e.g., copper)
- Electrostatic sprayers and fogging
- Hand and surface sanitizers/films with “residual” activity
- UV-C and ozone
- HEPA filtration
- Textile treatments

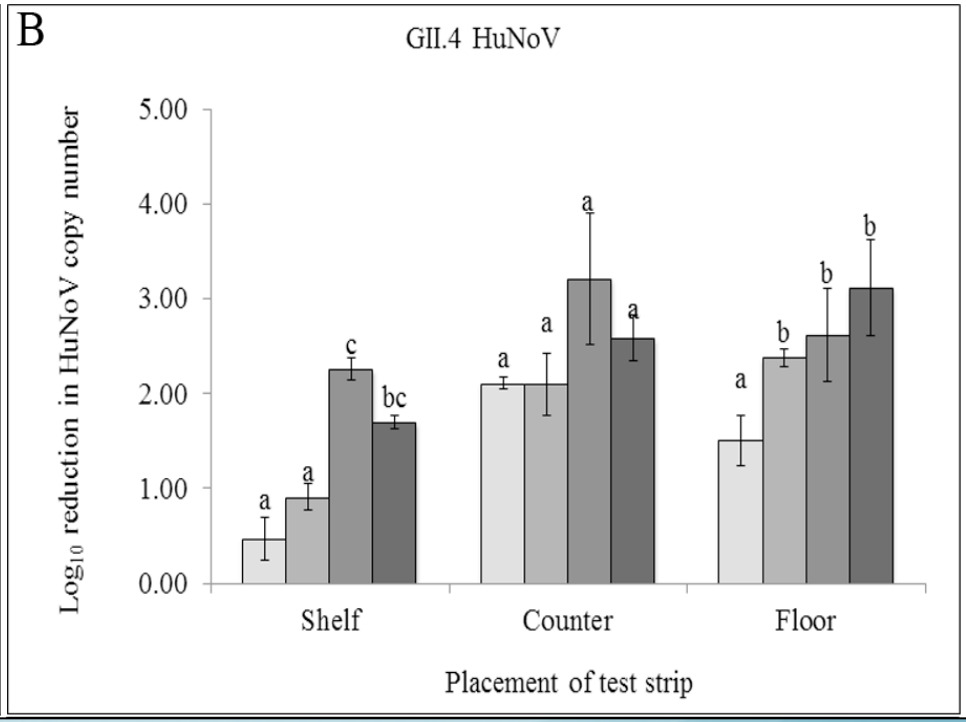


Virucidal Activity of Fogged Chlorine Dioxide- and Hydrogen Peroxide-Based Disinfectants against Human Norovirus and Its Surrogate, Feline Calicivirus, on Hard-to-Reach Surfaces

Naim Montazeri[1], Clyde Manuel[1], Eric Moorman[1], Janak R. Khatiwada[2], Leonard L. Williams[2] and Lee-Ann Jaykus[1]*

frontiers in Microbiology



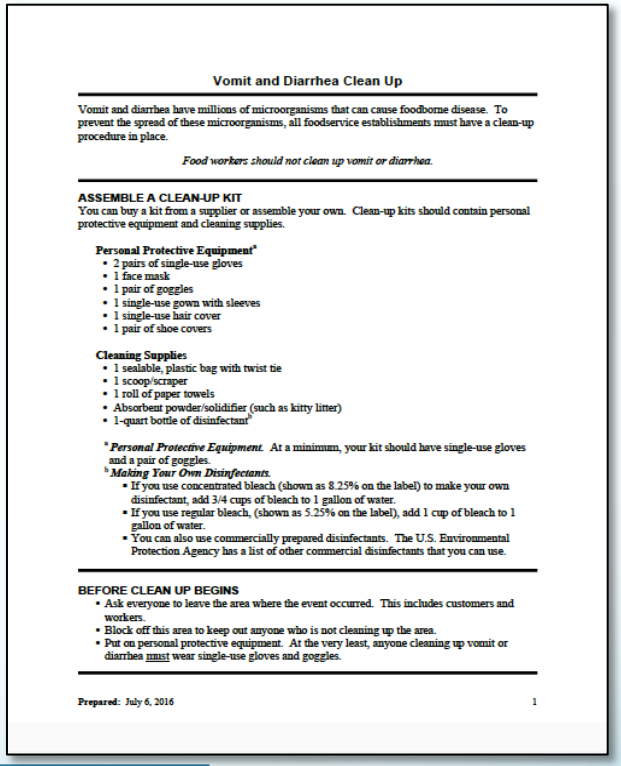


Evaluation Criteria

- Licensing for label claims?
- HUMAN norovirus (not surrogates)
- ‘Standardized’ assays
- Need DATA!
  - Strains
  - Study design
  - Multiple experimental methods to characterize infectivity
- Don’t get pulled into the hype
- Ask for proof

Clean-Up Guidelines

- Evidence-based
- Detailed procedural steps for vomit and fecal matter clean-up
- Editable and customizable for the facility
- Resulted in revised Section C of the Food Code requiring **written** clean-up documents for vomiting and fecal contamination events



Vomit and Diarrhea Clean Up

Vomit and diarrhea have millions of microorganisms that can cause foodborne disease. To prevent the spread of these microorganisms, all foodservice establishments must have a clean-up procedure in place.

Food workers should not clean up vomit or diarrhea.

ASSEMBLE A CLEAN-UP KIT

You can buy a kit from a supplier or assemble your own. Clean-up kits should contain personal protective equipment and cleaning supplies.

Personal Protective Equipment[a]
- 2 pairs of single-use gloves
- 1 face mask
- 1 pair of goggles
- 1 single-use gown with sleeves
- 1 single-use hair cover
- 1 pair of shoe covers

Cleaning Supplies
- 1 sealable, plastic bag with twist tie
- 1 scoop/scraper
- 1 roll of paper towels
- Absorbent powder/solidifier (such as kitty litter)
- 1-quart bottle of disinfectant[b]

[a] ***Personal Protective Equipment.*** At a minimum, your kit should have single-use gloves and a pair of goggles.

[b] ***Making Your Own Disinfectants.***
- If you use concentrated bleach (shown as 8.25% on the label) to make your own disinfectant, add 3/4 cups of bleach to 1 gallon of water.
- If you use regular bleach, (shown as 5.25% on the label), add 1 cup of bleach to 1 gallon of water.
- You can also use commercially prepared disinfectants. The U.S. Environmental Protection Agency has a list of other commercial disinfectants that you can use.

BEFORE CLEAN UP BEGINS
- Ask everyone to leave the area where the event occurred. This includes customers and workers.
- Block off this area to keep out anyone who is not cleaning up the area.
- Put on personal protective equipment. At the very least, anyone cleaning up vomit or diarrhea must wear single-use gloves and goggles.

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Conclusions

- Prevention (P) will lower risk more than will Inactivation (I)
- There are scientifically-valid reasons for interventions
  - Exclusion of ill workers (P)
  - Preventing bare hand contact with RTE foods (P)
  - Hand-hygiene (washing) (P and I)
  - Surface sanitizing and disinfecting (I)
  - Vomit/fecal matter cleaning guidelines (I)
- Regulatory changes needed relative to licensing for anti-hNoV claims
- Need for better actives and product formulations for:
  - Surface sanitizing and disinfecting
  - Hand hygiene
  - Proactive controls
- Clean before disinfecting/sanitizing
- Education of essential workforce


NOROVIRUS
YOU DON'T WANT IT