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Isolation needs for patients with ESBL: Summary

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Specific Care Question

Are criteria necessary to stop contact precautions (CP) in patients diagnosed with ESBL?

Recommendations Based on Current Literature (Best Evidence) Only

A conditional recommendation is made for ceasing the use of contact precautions (CP) for patients diagnosed with ESBL based on expert review of current literature by the Department of EBP. The overall certainty in the evidence is very low^a. The data reported in four studies are incorporated into this report. Based on the study findings, transmission rates of ESBL did not increase significantly after organizations supplanted CP with the use of standard precautions (SP), when caring for patients diagnosed with ESBL.

Literature Summary

Background. ESBL is an enzyme found in some strains of bacteria which have the ability to break down and destroy beta-lactam antibiotics (Centers for Disease Control and Prevention, 2019). ESBL was initially identified as a Hospital Acquired Infection (HAI) due to outbreaks within intensive care units however, the epidemiology has changed to include both HAI and community onset infections (Centers for Disease Control and Prevention, 2019; van Hout et al., 2020). As this disease is spread through the contact of infected human or animal fecal material, hospitalized patients have historically been isolated with CP for each admission after being diagnosed with this disease. However, new literature suggests that patients do not need to be placed in CP. This review will summarize identified literature to answer the specific care question.

In addition to the literature review, an informal city-wide survey (N = 12), of the Association for professionals in Infection Control and Epidemiology members (Y. Ballam, personal communication, February 3, 2020), identified that isolation practice is variable when caring for this patient population:

- four organizations isolate with CP for duration of stay,
- three organizations use one or two negative ESBL cultures to determine if CP can be removed,
- two organizations employ CP each time the patient is admitted,
- one organization employs CP for six months from diagnosis,
- one organization uses CP if the patient has an active uncontained infection, and
- one organization does not isolate patients diagnosed with ESBL.

Study characteristics. The search for suitable studies was completed on February 3, 2020. Y. Ballam, BS, CIC; R. Mott, MSN, FNP-BC, CIC, APRN; and S. McCullough-Culer, MPH, BSN, RN, CIC reviewed the 23 titles and/or abstracts^b found in the search. No guidelines were found to answer the question, but nine single studies were believed to answer the question. After an in-depth review of the nine articles^c, four answered the question. All four studies (Jalalzaï et al., 2018; Renaudin et al., 2017; Thompson, Teter, & Atrubin, 2020; Tschudin-Sutter et al., 2016) employed a before and after cohort methodology (see Figure 1) to measure the effect of discontinuing CP for patients with a history of ESBL.

Summary by Outcome

Incidence of HAI with ESBL. Four studies (Jalalzaï et al., 2018; Marra, Edmond, Schweizer, Ryan, & Diekema, 2018; Renaudin et al., 2017; Thompson et al., 2020; Tschudin-Sutter et al., 2016) reported ESBL transmission in two ways: Incidence rates of health care associated ESBL infection (Jalalzaï et al., 2018; Thompson et al., 2020; Tschudin-Sutter et al., 2016) and incidence density rates (Renaudin et al., 2017). The total population for the included studies, nor the reported study findings, could not be pooled due to how the data was reported (a) two studies (Jalalzaï et al., 2018; Renaudin et al., 2017) reported the sample size as patients, (b) Tschudin-Sutter et al. (2016) reported only contact and index sample sizes, and (c) Thompson et al. (2020) described the sample size as laboratory specimens.

Jalalzaï et al. (2018) reported an insignificant finding (p = 0.94) that ICU acquired ESBL infections accounted for 5.2% and 5.5%, before and after, ceasing active surveillance ESBL cultures. Renaudin et al. (2017) reported a significant (p = .004) nonsuperiority incidence density finding for ESBL in the ICU before and after ceasing CP 2.7, 95% CI [1.78, 3.62] and 2.06, 95% CI [1.27, 2.86] per 1,000 patient days, respectively. Thompson et al.

Children's Mercy If you have questions regarding this Specific Care Question – please contact <u>infectionpreventioncontrol@cmh.edu</u> KANSAS CITY

(2020) described a significant decrease (p = .022) when comparing health care-associated ESBL rates before and after eliminating CP 3.71 per 10,000 patient days versus 3.00 per 10,000 patient days, respectively. Tschudin-Sutter et al. (2016) reported a transmission rate of 2.6% after CP were removed for patients with ESBL. These findings indicate that removal of CP in patients diagnosed with ESBL does not significantly (p = .052) increase transmission rates when SP are followed.

Certainty of the evidence for HAI with ESBL. The certainty of the body of evidence is based on four factors: within-study risk of bias, consistency among studies, directness of evidence, and precision of effect estimates. The body of evidence was assessed to have very serious risk of bias, and very serious inconsistency. The risk of bias was assessed to be very serious as the four included studies employed a cohort methodology which may have influenced the study findings through uncontrolled confounding variables. The assessment of very serious inconsistency was attributed to the body of literature as different populations and outcome measures were reported.

Identification of Studies

Search Strategy and Results (see Figure 1)

Search: ((("beta-Lactamases"[MeSH] OR "beta-Lactam Resistance"[Mesh]) AND ("Enterobacteriaceae Infections"[Mesh] OR "Enterobacteriaceae"[MeSH])) OR "Drug Resistance, Multiple, Bacterial" [mesh] OR extended-spectrum β -lactamase OR extended-spectrum β -lactamase OR ESBL-producing E. coli OR ESBL OR extended-spectrum β -lactamase (ESBL) producing organisms OR extended-spectrum β -lactamase) AND (((screen OR screening OR Isolation OR "Transmission-based precautions" OR "contact precautions" OR "infection control" OR effectiveness[tiab]) AND (Cessation OR discontinue OR discontinuation OR discontinue)) OR (Return to Standard Precautions) OR "universal contact precautions") Records identified through database searching n = 23

Studies Included in this Review

Citation	Study Type
Jalalzaï et al. (2018)	Before/After cohort
Renaudin et al. (2017)	Before/After cohort
Tschudin-Sutter et al. (2016)	Before/After cohort
Thompson et al. (2020)	Before/After cohort

Studies Not Included in this Review with Exclusion Rationale

Citation	Reason for exclusion		
Johnson and Quach (2017)	Narrative review		
Marra et al. (2018)	Systematic review which reported the findings from Tschudin-Sutter et al. (2016) as this article is reported as a single study this review was excluded from this report.		
Metan et al. (2017)	Letter to the editor		
Prevel et al. (2019)	Titled as a systematic review but it was a narrative review		
van den Bijllaardt et al. (2018)	Studied the performance of ESBL PCR as a screening assay for ESBL carriage		

Methods Used for Appraisal and Synthesis

^a<u>The GRADEpro Guideline Development Tool (GDT)</u> is the tool used grade the overall body of literature for this analysis.

^bRayyan is a web-based software used for the initial screening of titles and / or abstracts for this analysis (Ouzzani, Hammady, Fedorowicz & Elmagarmid, 2017).

^cReview Manager (Higgins & Green, 2011) is a Cochrane Collaborative computer program used to assess the study characteristics as well as the risk of bias and create the forest plots found in this analysis.

dThe Preferred Repor	ting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram depicts the process in which literature is searched,		
screened, and eligibility criteria is applied (Moher, Liberati, Tetzlaff, & Altman, 2009).			
^a GRADEpro GDT: GRADEpro Guideline Development Tool (2015). McMaster University, (developed by Evidence Prime, Inc.). [Software]. Available			
from <u>gradepro.org</u> .			
^D Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan-a web and mobile app for systematic reviews. Systematic Reviews, 5(1),			
210. doi:10.1186/s13643-016-0384-4			
^c Higgins, J. P. T., & C	Green, S. e. (2011). Cochrane Handbook for Systematic Reviews of Interventions [updated March 2011] (Version 5.1.0 ed.): The		
Cochrane Coll	aboration, 2011.		
"Moher D, Liberati A,	Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA		
Statement. PLoS	Med 6(7): e1000097. doi:10.1371/journal.pmed1000097 For more information, visit <u>www.prisma-statement.org</u> .		
Question Originato	r		
Bobbi Mott, MSN	, FNP-BC, CIC, APRN		
Medical Librarian R	lesponsible for the Search Strategy		
Keri Swaggart, M	ILIS, AHIP		
EBP Scholar/Team	Member Responsible for Analyzing the Literature		
Nancy Allen, MS,	MLS, RD, LD, CPHQ		
Linda Martin, RN,	BSN, CPAN		
Robyn McCracker	I, RRT, NPS		
Anthony Randall,	MHA, RRT, RRT-ACCS, RRT-NPS, C-NPT, CPPS		
Kim Robertson, N	1BA, MI-BC		
Asnley Wilson, B	SN, KN, CPN		
EBP leam Member	Responsible for Reviewing, Synthesizing, and Developing this Document		
Jacqueime A. bar	ueu, PND, RN		
Acronyms Used in thi	is Document		
Acronym	Explanation		
ASC	Active Surveillance Cultures		
CAT	Critically Appraised Topic		
CP	Contact Precautions		
CRE	Carbapenem-resistant Enterobacteriaceae		
EBP	Evidence Based Practice		
ESBL	Extended-Spectrum Beta-Lactamase		
FPH	Felix Platter Hospital		
HAI	Hospital Acquired Infection		
ICU	Intensive Care Unit		
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses		
SP	Standard Precautions		
UHB	University Hospital Based		
Date Developed			
April 2020			





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Characterisits of Intervention Studies Jalalzaï et al. (2018)

Characteristics of Study	
Methods	Cohort, Pre and Post Intervention
Participants	 Participants: Adult patients admitted to the intensive care unit (ICU) during two 1-year periods: Group 1, Pre-intervention, Active surveillance cultures (ASC) timeframe: 4.1.2013 to 3.31.2014 Group 2, Post-intervention, No active surveillance cultures (no-ASC) timeframe: 9.1.2014 to 8.31.2015 (timeframe began 6 months after ASC cessation) Setting: 18 bed medical-surgical ICU in a teaching hospital in France. Number in study: N = 1069 Group 1: n = 524 Group 2: n = 545 Gender, males: (as defined by researchers) Group 1: n = 321 (61.2%) Group 1: n = 321 (61.6%) Race / ethnicity or nationality (as defined by researchers): The study occurred in France. The authors did not identify race or ethnicity of the participants. Age, median in years, IQR Group 1: 65, 54-76 Group 2: 64, 52-75 Inclusion criteria: Patients with a first ICU stay of more than two calendar days Exclusion criteria: Not reported Covariates identified: Not reported
Interventions	 Both: Pre-intervention: Patients routinely screened for ESBL carriage by rectal swabbing at admission then weekly afterwards. Post-intervention: Policy of systematic screening for ESBL carriage withdrawn.



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Outcomes	Primary outcomes:				
	Incidence of ICU-acquired ESBL-E infections*				
	 Imported carriage was defined as a po 	sitive rectal swab within t	he 48 hours followir	ig admission	
	• Acquired carriage was defined as a positive surveillance swab in patients with a negative admission sample				
	 Overall carbapenem consumption* 		-		-
	 Patient outcomes* 				
	Secondary outcome:				
	Not reported				
	Safety outcome:				
	Not reported				
	*Outcomes of interest to the CMH CAT development te	eam			
Results	Incidence of ICU-acquired ESBL-E infections				
	 863 rectal swabs total for ASC period (admissi 	on = 524; weekly surveill	ance = 339		
	 28 (5.3%) were identified as ESBL-E c 	arriers			
	 17 (3.2%) with imported carrie 	age			
	 11 (2.1%) with ICU-acquired of 	arriage			
	The cumulative incidence of ICU-acquired ESB	L-E infections did not diffe	er between periods		
		ASC period $(n - 524)$	No-ASC period $(p - 545)$	p value	
	ESBL-E ICU acquired infections	$\frac{(n-324)}{6(1.1\%)}$	$\frac{(1-5+5)}{8(1-5\%)}$	64	
	Incidence density per 1,000 patients-days	1.2 (6/4.823)	1.4 (8/5.608)	.80	
	Overall carbapenem consumption				
	Overall carbapenem exposure in patients with	no ICU-acquired ESBL-E i	nfection decreased	between ASC p	period and
	no-ASC period (75 versus 62 carbapenem-day	s per 1000 patients, respe	ectively, $p = .01$)		
		ASC period	No-ASC period	<i>p</i> value	
	All patients	81.5 (383/4823)	63.3 (355/5608)	.03	
	No ICU-acquired ESBL-E infection				
	Overall	75 (353/4705)	61.9 (315/5088)	.01	
	 No ESBL-E carriage 	66 (281/4260)			
	ESBL-E carriage	161.8 (72/445)			
	ICU-acquired ESBL-E infection	339 (40/118)	273.1 (142/520)	.15	

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	All patients $n = 1069$	ASC period $n = 524$	No-ASC period n = 545	p value
ICU median length of stay (IQR), days	6 (4-11)	6 (4-11)	6(4-11)	.82
Hospital median length of stay (IQR), days	16 (8-27)	16 (9-27)	16 (8-29)	.89
In-ICU mortality, n (%)	220 (20.6)	101 (19.3)	119 (21.8)	.30
Hospital mortality, \vec{n} (%)	272 (25.4)	130 (24.8)	142 (26.1)	.64

Renaudin et al. (2017)

Characteristics of Study	
Methods	Cohort, Pre and Post Intervention
Participants	Participants: Adult patients in an ICU before, when contact isolation precautions were in place, and after when SP were in
	place
	Setting: An intensive care unit in France
	Number enrolled into study: $N = 3,124$
	• Group 1, CP: n = 1,54/
	• Group 2, SP: $n = 1,577$
	Number completed: $N = 3,124$
	• Group 1, CP: n = 1,54/
	• Group 2, SP: n = 1,577
	Gender, males: (as defined by researchers)
	• Group 1, CP: n = 59.5%
	• Group 2, SP: $n = 60.8\%$
	Race / ethnicity or nationality (as defined by researchers):
	• The study occurred in France. The authors did not identify race or ethnicity of the participants.
	Age, mean, years (SD)
	• Group 1, CP: $n = 65.3 (16.3)$
	• Group 2, SP $n = 62.9 (16.1)$
	Inclusion criteria:
	All patients admitted to the hospital's ICU
	• Group 1, CP: January 1, 2012 to January 31, 2014
	• Group 2, SP: February 1, 2014 to February 29, 2016
	Liciusion criteria.
	• Hand bygione compliance
	 Natification of all nations supporting health care providers of changes of presoutions
	• Notification of all patient supporting health care providers of changes of precautions
	 Aller Feb 2014 - Use of action training, or immediate corrective actions, for all healthcare provider and newcomers on WHO.
	hand hygiene recommendations,
	 Compliance to selection, donning, and doffing PPE per hospital standard



Interventions	CP: These were discontinued from February 1, 2014 onward for patients colonized or infected with MRSA or ESBL
	Hand hygiene on entering and leaving the room
	 Wear gloves when touching the patient's skin or items in close proximity to the patient
	Wear gown if anticipating your clothing will touch the patient's items potentially contaminated surfaces
	• Use patient-dedicated or single use disposable equipment, or clean and disinfect shared equipment between
	patients, eq blood pressure cuffs
	SP:
	Hand hygiene with alcohol-based hand rub before and after patient/ patient environment contact
	Wearing PPF if contact with blood or body fluids was a risk
	 Notification of all patient supporting health care providers of changes of precautions
Outcomes	
Outcomes	Definitions:
	 ICU- acquired case of MRSA or ESBL defined if the first positive culture occurred ≥ 48 hours of ICU admission
	Carriage at admission if positive culture(s) occurred prior to 48 hours
	Primary outcome:
	 Incidence density of ICU acquired MRSA or ESBL* per 1,000 patient days
	Secondary outcomes:
	Incidence of carriage of MRSA or ESBL at admission
	 Antibiotic consumption reported guarterly as defined daily dose (DDD)/1,000 patient days
	Compliance to hand hygiene protocols - Use of alcohol-based hand-rub reported as liters/1.000 patient days
	Compliance to selection, donning, and doffing PPE per hospital standard
	 Length of stay
	Safety outcome:
	Not reported
	• Not reported
	II™Outcomes of interest to the CMH CAT development team



Results	Statistics:
	For the incidence density of acquired and carriage MRSA or ESBL the noninferiority analysis was employed. Both were
	expected to have nonsuperior incidence during the standard precaution period.
	 Incidence densities were compared using Schuirmann's 2 one-sided test (<u>TOST</u>)
	 Margin of nonsuperiority for both was fixed at one multidrug-resistant organism per 1,000 patient days
	Results:
	Acquisition of MRSA in the ICU, incidence density was significantly nonsuperior during the standard precaution with
	a margin of $1/1,0000$ days, $p = .002$
	 Group 1, CP - 10 patients
	 Group 2, SP - 10 patients
	Acquisition of ESBL-E in the ICU, incidence density was significantly nonsuperior during the standard precaution
	period with a margin of $1/1,000$ patient days, $p = .004$
	o Group 1, CP - 33 patients
	o Group 2, SP - 26 patients
	• Carriage of MRSA at admission, incidence density was significantly noninferior during the standard precaution with a margin of $1/1,000$ patient days, $p = .05$
	 Carriage of ESLB at admission was not significantly different between periods
	 There was no significant difference in antibiotic consumption, alcohol-based hand-rub use, compliance to PPE selection and use standards, or length of stay

Thompson et al. (2020)

Characteristics of Study	
Methods	Cohort, Pre and Post Intervention
Participants	Participants: Hospitalized patients with extended-spectrum ß-lactamase-positive (ESBL) producing organism Setting: USA, Urban academic 1,010 bed medical center Number of laboratory results during study: N = 1,273 (January 2014-August 2017) Gender, males: (as defined by researchers) • The study occurred in 2020 in the United States. The authors did not identify gender of the participants. Race / ethnicity or nationality (as defined by researchers): • The study occurred in 2020 in the United States. The authors did not identify race or ethnicity of the participants. Age: • The study occurred in 2020 in the United States. The authors did not identify age of the participants. Inclusion criteria: • Positive laboratory result for ESBL organism Exclusion criteria: • Enterobacteriaceae that met definitions for either Carbapenem-resistant Enterobacteriaceae (CRE) or carbapenemase producer-CRE • Surgical site infection Covariates identified:
	Not reported

Interventions	Group 1: CP for ESBL-positive laboratory results Group 2: No CP for ESBL-positive (only) laboratory results			
Outcomes	 Primary outcome: Incidence of healthcare acquired infection (HAI) with ESBL-positive laboratory results* Secondary outcome: Number of patients not being placed in CP Safety outcome: Not reported *Outcomes of interest to the CMH CAT development team 			
Results	 Reported 387 cases of HAI with ESBL infections during the entire study time frame. Pooled ESBL incidence density rate decreased from 3.71 per 10,000 patient days to 3.0 per 10,000 patient days. Documented HAI associated ESBL infection after discontinuation of CP was 25% Lower compared with the baseline period (<i>p</i> < .001). The Durbin-Watson statistic confirmed no autocorrelation (Durbin-Watson = 2.11) and the Dickey-Fuller unit root test confirmed stationarity of the outcome variable (tau, -6.54; <i>p</i> <.001) for the model. Approximately 378 patients with ESBL -positive organisms were not placed in isolation 			
	Pre-Intervention (January 2014 - November 2015)Post-Intervention (December 2015 - August 2017)p valueNumberNumberDenominatorRateNumberDenominatorRateCommunityPrevalenceRate (per370282 14513 114516299 98317 201001			
	10,000 patient encounters) 370 282,143 13.114 310 299,983 17.201 .001 HAI incidence rate [all organisms] (per 10,000 patient days) 221 595,336 3.712 166 553,748 2.998 <.001 Community Prevalence Rate (per 595,336 3.712 166 553,748 2.998 <.001			
	Community Prevalence rate (per 10,000 patient encounters) 370 282,145 13.114 516 299,983 17.201 .001 HAI incidence rate [all organisms] 221 595,336 3.712 166 553,748 2.998 <.001			



Tschudin-Sutter et al. (2016)

Characteristics of Study	
Methods	Cohort, Pre and Post Intervention
Participants	Participants: Hospitalized patients and long-term care facility patients Setting: University Hospital Basel (UHB) and affiliated long-term care center Felix Platter Hospital (FPH), Basel, Switzerland Number enrolled into study: N = 442 Group 1, Index Patients: n = 211 UHB Patients: n = 178 FPH Patients: n = 33 Group 2, Contact Patients: n = 231 UHB Patients: n = 151 FPH Patients: n = 80 Number completed: N = 442 Group 1: n = 211 Group 2: n = 231 Gender, males: Not reported Race / ethnicity or nationality (as defined by researchers): The study occurred in Switzerland. The authors did not identify race or ethnicity of the participants. Age: Not reported Inclusion criteria: Not reported Exclusion criteria: Not reported Covariates identified: Not reported
Interventions	Both: UHB and FPH abandoned routine CP for patients with extended-spectrum ß-lactamase (ESBL)-producing Eschericia coli
	 (E. coll) Group 1: Patients colonized or infected with an ESBL-producing <i>E. coli</i> Group 2: Patients hospitalized for at least 24 hours in the same room as an index patient Screened for ESBL-producing <i>E. coli</i> after a median contact time of 4 days at UHB and 15 days at FPH



Outcomes	Primary outcome:
	 ESBL- producing <i>E. coli</i> transmission rates*
	Secondary outcome:
	Contact time*
	Safety outcome:
	Not reported
	*Outcomes of interest to the CMH CAT development team
Results	 After discontinuing contact isolation precautions in shared hospital rooms where a patient with ESBL-producing <i>E.coli</i> (index patient) was exposed to a patient without the infection (contact patient) for at least 24 hours, transmission rates were 2.6% and 8.8% at an acute-care (UHB) and a geriatric/rehabilitation hospital (FPH), respectively. With the use of CP, the reported transmission rates were 1.5% at UHB, and 6.5% for similar settings to FPH (previous transmission rates for FPH specifically were not reported).
	 Exposure to an index patient for >5 days was associated with increased odds for transmission OR = 10.18, 95% CI [1.28, 80.91], p = .028



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