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Clinical Studies

Antenatal and intrapartum nucleic acid amplification test use for group B *Streptococcus* screening—United States, 2016☆,☆☆,★

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ABSTRACT

Perinatal group B *Streptococcus* (GBS) disease prevention guidelines in 2010 allowed for processing of screening specimens by nucleic acid amplification tests (NAATs); however, the extent of NAAT use is unknown. A 2016 laboratory survey sent to 10 surveillance sites found that 18.7% of responding laboratories offered NAAT for GBS screening (antenatal only: 7.3%; intrapartum only: 4.1%; both: 3.4%).

Group B *Streptococcus* (GBS) remains a leading cause of neonatal illness and death in the United States despite an 80% decline in disease in the first week of life (early-onset disease) due to screening and intrapartum antibiotic prophylaxis (IAP) (Schrag and Verani, 2013). Since 2002, GBS disease prevention guidelines have recommended universal antenatal GBS screening of pregnant women at 35–37 weeks' gestation, with IAP for colonized women and those with unknown GBS status and presence of specific clinical factors (ACOG, 2002; Verani et al., 2010). Culture-based screening methods are effective but require 48 to 72 h for results and thus are of limited utility in the intrapartum (during labor and delivery) setting. Currently licensed nucleic acid amplification tests (NAATs) can yield results in 1 to several hours, but require an 18–24-h enrichment step to achieve sensitivity similar to culture. In 2010, guidelines were updated to allow for processing of antenatal screening specimens by NAATs following an enrichment step. Given the greater value of rapid results within the intrapartum setting, the update allowed for NAAT testing of intrapartum specimens without an enrichment step for women with unknown GBS status and no other prophylaxis indications (Verani et al., 2010) even though some studies show reductions in sensitivity to as low as 63% (Atkins et al., 2006; Aziz et al., 2005; Scicchitano and Bourbeau, 2009). Before 2010, 3 FDA-licensed NAAT systems were available with limited uptake—0.2% antenatal and <3% intrapartum (Van Dyke et al., 2009). We characterized antenatal and intrapartum GBS NAAT use in 2016.

The Active Bacterial Core Surveillance (ABCs) is a laboratory and population-based surveillance for invasive bacterial pathogens including GBS in selected counties of 10 U.S. states (CA, CO, CT, GA, MD, MN, NM, NY, OR, and TN), with a total population of 400,000 live births annually. All the clinical laboratories that serve residents of each surveillance site (either the entire state or a defined subset of counties) are queried actively for sterile site isolations of the ABCs pathogens. These sites distribute an annual survey using REDCap, a secure web application for database management, to laboratories serving the catchment to characterize current testing practices, with a focus on laboratories that process sterile-site samples. In 2016, additional questions were added regarding GBS antenatal and intrapartum NAAT use. Descriptive statistics were assessed by individual site and in aggregate. Live birth data from 2012 were used to estimate the proportion of births occurring in facilities that used NAATs for GBS intrapartum screening.

Over 93% (507/544) of laboratories responded to the survey. Ninety-five out of 507 (18.7%) laboratories used GBS NAATs (antenatal screening only: 7.3%; intrapartum screening only: 4.1%; both antenatal and intrapartum screening: 3.4%; Table 1). The majority (87.4%) were

☆ Article Tweet: Survey finds increasing use of rapid screening tests for #groupBstrep during pregnancy & delivery in the US, but a more accurate & simple bedside test is needed to better protect newborns from GBS disease. #GBSaware.

☆☆ Declarations of interest: none.

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Table 1
Characteristics of laboratories that indicated use of nucleic acid amplification tests for GBS screening, 2016.

	Total ($n = 95$)	Antenatal only ($n = 37$)	Intrapartum only ($n = 21$)	Both antenatal and intrapartum ($n = 17$)	Context not specified ($n = 20$)
Type of facility					
Hospital/clinical laboratory	83 (97.4)	33 (89.1)	21 (100)	16 (94.1)	13 (65)
Commercial/private laboratory	12 (12.6)	4 (10.8)	0 (0)	1 (5.9)	7 (35)
Type of system used					
Cepheid Genexpert	58 (61.5)	23 (62.2)	20 (95.2)	10 (58.8)	5 (25)
Illumigene	9 (9.5)	6 (16.2)	0 (0)	1 (5.9)	2 (10)
BD Max GBS	8 (8.4)	4 (10.8)	0 (0)	2 (11.8)	2 (10)
Other	11 (11.6)	3 (8.1)	1 (4.8)	3 (17.6)	4 (20)
Unknown	9 (.5)	1 (2.7)	0 (0)	1 (5.9)	7 (35)

hospital or clinical laboratories. The proportion of laboratories using NAATs varied by state, with antenatal use ranging from 1.3% (GA) to 16.7% (CO) and intrapartum use ranging from 2.6% (GA and OR) to 8.7% (MD). The rate of early-onset GBS disease also varied by site (OR: 0.44; CA: 0.02, Table 2). Less than 10% of live births within the ABCs catchment area occurred at hospitals affiliated with laboratories offering intrapartum NAATs for GBS; this ranged from 2.9% of live births in the CA site to 34.1% of live births in the NY site (Table 2). The most common NAAT system used was the Cepheid GeneXpert (61.5%) followed by Illumigene (9.5%) and BD Max GBS (8.4%) (Table1). Most (82%) laboratories that used NAATs for antenatal screening performed the test after an enrichment step (Table 2). Half (50%) of the laboratories that reported use of NAAT for intrapartum screening reported a turnaround time of 1–2 h, and roughly one-third (29%) reported a turnaround time of less than 1 h (Table 2).

GBS NAAT use has increased since the 2010 GBS update but still remains limited. Currently, 8 GBS NAAT systems from 6 companies are licensed by the FDA. As clinical laboratories scale back culture-based methods, these platforms allow for workflow efficiencies and decreased hands-on processing time. Within the antenatal setting, however, licensed NAATs still require a lengthy enrichment phase to achieve a sensitivity similar to culture (Davies et al., 2004). Furthermore, available NAATs do not provide macrolide susceptibilities to inform agent choice for GBS-colonized women who cannot receive first-line beta-lactam prophylaxis. This is particularly important as GBS resistance to clindamycin and erythromycin has been increasing over the past several decades, with the prevalence of resistance invasive GBS isolates up to 21% for constitutive clindamycin and 45% for erythromycin as of 2015 (Nanduri, 2018).

In the intrapartum setting, a simple, rapid screening test holds promise for advancing GBS disease prevention. Almost two-thirds [61.4% in 1 multistate study (Van Dyke et al., 2009)] of early-onset GBS cases in the era of universal antenatal screening occur among infants of women who screened negative at 35–37 weeks' gestation, reflecting both suboptimal specimen collection and processing and true changes in colonization status between screening and delivery. When evidence was reviewed during the 2010 GBS guidelines revision, available GBS NAATs did not have adequate simplicity or sensitivity in the absence of enrichment to allow for intrapartum NAAT screening to replace antenatal screening. Moreover, the intrapartum setting demands a more rapid turnaround time than the current 1–2 h (Aziz et al., 2005; Plainvert et al., 2018), as beta-lactam IAP is over 91% effective when administered 4 or more hours before delivery but loses effectiveness when administered closer to delivery (Fairlie et al., 2013).

Although the survey included laboratories from 10 states that served approximately 10% of the U.S. population, it may not represent national practices. While these results suggest geographic variation, particularly in the availability of intrapartum GBS NAATs, the sample size of surveyed laboratories was small in some states. Also, laboratories that do not process sterile site samples may have been underrepresented. Finally, surveyed laboratories were not asked to provide standard operating procedures or summary data on samples processed to determine accuracy of survey responses. Thus, while characterization of use is possible, accuracy and quality of results are unknown.

Current NAAT platforms for GBS screening are not adequate to replace culture-based testing methods during the antenatal period. A NAAT that can detect GBS resistance to macrolides in addition to the presence/absence of GBS would be beneficial. In the intrapartum setting, an ideal screening test should be highly sensitive and specific, be simple enough for labor and delivery staff to perform, have a turnaround time of less than 30 min, and provide antimicrobial susceptibility information needed for appropriate IAP agent choice, which current NAAT testing platforms are unable to do. If this could be achieved, intrapartum NAAT screening holds promise to replace antenatal screening and potentially further reduce the burden of early-onset neonatal GBS disease.

Table 2
Antenatal GBS NAAT enrichment procedures, intrapartum GBS NAAT turnaround times, proportion of live births with access to laboratories offering intrapartum GBS NAAT, and rates of early-onset GBS disease by ABCs area, 2016.

	Total	CA	CO	CT	GA	MD	MN	NM	NY	OR	TN
Laboratories using antenatal GBS NAAT	($n = 54$)	($n = 1$)	($n = 3$)	($n = 3$)	($n = 1$)	($n = 7$)	($n = 21$)	($n = 3$)	($n = 7$)	($n = 2$)	($n = 6$)
After enrichment step, *n* (%)	44 (82)	0 (0)	2 (67)	3 (100)	1 (100)	6 (86)	20 (95)	3 (100)	7 (100)	1 (50)	1 (17)
Without enrichment step, *n* (%)	9 (17)	1 (100)	1 (33)	0 (00)	0 (0)	1 (14)	1 (5)	0 (0)	0 (0)	0 (0)	5 (83)
Unknown, *n* (%)	1 (1.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)
Laboratories offering intrapartum GBS NAAT	($n = 38$)	($n = 1$)	($n = 2$)	($n = 1$)	($n = 2$)	($n = 7$)	($n = 14$)	($n = 3$)	($n = 4$)	($n = 2$)	($n = 2$)
Turnaround time <1 h, *n* (%)	11 (29)	0 (0)	2 (100)	0 (0)	0 (0)	4 (57.1)	2 (14.2)	1 (33.3)	0 (0)	1 (50)	1 (50)
Turnaround time 1–2 h, *n* (%)	19 (50)	1 (100)	0 (0)	1 (100)	2 (100)	3 (42.9)	9 (64.2)	2 (66.7)	0 (0)	0 (0)	1 (50)
Turnaround time >2 h, *n* (%)	7 (18)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (21.4)	0 (0)	4 (100)	0 (0)	0 (0)
Unknown, *n* (%)	1 (2.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)
Total live births in catchment area, 2012	431,626	38,667	30,239	36,203	69,689	72,751	65,293	25,391	22,728	20,360	50,305
Occurring at hospitals affiliated with laboratories	39,280	1, 127	3412	2215	5135	21,021	15,612	1269	7761	2749	4175
offering intrapartum NAAT, *n* (%)	(9.1)	(2.9)	(11.3)	(6.1)	(7.4)	(28.9)	(23.9)	(4.9)	(34.1)	(13.5)	(8.3)
Rate of early-onset GBS cases, 2016[a] (per 1000 live births)	0.23	0.02	0.12	0.17	0.36	0.23	0.3	0.39	0.04	0.44	0.18

[a] Rates calculated using total live births in catchment area in 2015.

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