decreased in patients with inflammation of the compartment beyond CD(i.e., amnionitis, chorionic plate inflammation or funisitis)(711.9,[7.6-10897.4] vs. 321.1,[3.0-5555.0] vs. 124.9,[2.2-4533.9]; P<.05), but not inflammation restricted to the chorio-decidua(19.0,[1.9-2586.7] vs. 22.1,[4.0-1257.4] vs. 12.5,[3.9-1075.3]; P>.1), with GA. Furthermore, there was a significant inverse relationship between GA and UCP CRP concentrations at birth in patients with funisitis(r=-0.280, P<.0005) and inflammation of the compartment beyond CD(r=-0.253, P=.005).

CONCLUSION: UCP CRP concentrations at birth in the context of funisitis, but not acute-HCA without funisitis, distinctly decrease throughout preterm-gestation. This finding suggests that FIR decreases even in the same setting of funisitis with increasing GA.

185 The impact of copy number analysis in expanded carrier screening

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OBJECTIVE: To examine the impact of copy number variants (CNVs) on detection rates in expanded carrier screening (ECS) panels.

STUDY DESIGN: ECS panels typically include analysis of copy number variation (CNV) for only a small subset of genes and exons, often to the detriment of detection rate. To assess the impact of panel-wide CNV analysis, a preliminary analysis was performed on 56,267 de-identified ECS tests performed by full-exon next-generation sequencing at Counsyl's laboratory. A 93 gene subset (consisting of severe and profound diseases) of Counsyl's ECS panel was analyzed to estimate the additional benefit of copy number analysis. The disease risk, i.e., the probability that a hypothetical child from randomly selected parents is affected by disease, was used as a metric for detection rate. No variant curation was performed on the detected CNVs and all detected deletions/duplications were assumed pathogenic. To calculate the disease risk, historical NGS data at Counsyl was used to estimate deleterious allele frequencies (AFs). The AFs were then used to calculate the disease risk with CNV estimates either excluded or included.

RESULTS: Without CNV analysis, the disease risk of the 93 gene subpanel was 123 affected children per 100,000. The addition of CNV analysis increased the detection rate by 2.0%, to 125 affected children per 100,000. This change in disease risk is roughly equivalent to calling non-CNV variants via NGS in the 54 least prevalent genes, which contribute 2.0% of the observed disease risk.

CONCLUSION: Panel-wide CNV analysis increases detection rate and provides more value than the addition of low-prevalence genes. CNV calling may be important to further reduce a patient's residual risks for specific genes due to certain scenarios, e.g., family history of a genetic disease and partner testing of known carriers for recessive diseases. For example, in HBB, CFTR, and ATM, CNVs account for up to 9% of the total detection rate. Further work to assess the clinical impact of the discovered variants is ongoing.

186 Non-invasive prenatal testing (NIPT) versus diagnostic testing for evaluation of fetal structural anomalies

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OBJECTIVE: Fetal structural anomalies are associated with whole chromosome aneuploidy and sub-chromosomal copy number variants (CNVs) in approximately 3-6% of cases. Although the recommended evaluation of a fetus with an anomaly is diagnostic testing with microarray analysis, many physicians are offering non-invasive prenatal testing (NIPT) in cases where patients wish to avoid an invasive diagnostic procedure. This analysis evaluates the hypothetical performance of NIPT in this scenario.

STUDY DESIGN: This is a secondary analysis of 2 NICHD funded prospective studies evaluating the frequency of aneuploidy and CNVs diagnosed in utero. We determined the frequency of cytogenetic abnormalities in fetuses with structural anomalies (including NT ≥3.5mm). We calculated the ability of either single nucleotide polymorphism (SNP) based NIPT or massively parallel sequencing (MPS) based NIPT to identify these abnormalities. We assumed that SNP-based NIPT could identify all cases of trisomies 13, 18, 21, sex chromosome abnormalities, triploidy and deletions of 1p36, 4p, 15q11, and 22q11.2. MPS-based expanded NIPT was assumed to detect all trisomies and CNVs ≥7Mb as well as deletions of 1p36, 4p, 5p, 8q24, 11q23, 15q11.2, 17p11.2, and 22q11.2.

RESULTS: There were 1,724 fetuses with structural anomalies, 317 (18.4%) of which had an abnormal karyotype, and 106 (3.5%) of which had a pathogenic CNV. Among these, 1,294 had an isolated structural anomaly and 430 had multiple anomalies. Table 1 shows the cytogenetic abnormalities. SNP-based NIPT would identify 79.1% of the abnormalities and MPS-based would identify 87.4%. Detection rates vary by specific organ system, as shown in Table 2.

CONCLUSION: An expanded MPS-based and a SNP-based NIPT could potentially identify 87.4% and 79.1%, respecitively, of cytogenetic abnormalities among fetuses with structural anomalies. However, this assumes that NIPT has 100% detection of all intended anomalies. Accordingly, its detection in clinical practice will be less. Patients choosing NIPT as their primary genetic test for a structural abnormality must be informed of his limitations.

Table 1: Cytogenetic abnormalities and abnormalities identifiable by NIPT

	N	All cytogenetic abnormalities, n (%)	Common aneuploidies, n (%)*	Triploidy, n (%)	Pathogenic CNVs, n (%)				Abnormalities identifiable by NIPT, n (%)	
					>7Mb**	≤7Mb	22q11.2 del	Other Targeted Deletions***	SNP-based	MPS-based
All anomalies	1724	436 (25.3)	317 (18.4)	13 (0.7)	49 (2.8)	57 (3.3)	14 (0.8)	1 (0.0)	345 (79.1)	381 (87.4)
Multiple anomalies	430	161 (37.4)	109 (25.3)	8 (1.9)	18 (4.2)	26 (6.0)	8 (1.9)	0 (0.0)	125 (77.6)	135 (83.9)
Single anomaly	1294	275 (21.2)	208 (16.1)	5 (0.4)	31 (2.4)	31 (2.4)	6 (1.4)	1 (0.0)	220 (80.0)	246 (89.5)

* Includes trisomy 21,18,13, sex chromosome abnormalities
** Includes rare aneuploidies, CNVs > 7mb and 23 mosaic rare aneuploidies
***15q11, 11q23, 8q24, 1p36, 4p-, 5p- (detectable by both SNP and MPSS)

Table 2: Cytogenetic abnormalities by organ system anomaly and potential NIPT detection

Organ System Anomalies	N	Any abnormality by microarray (%)	Abnormality identifiable by NIPT (%)	
			SNP-based	MPS-based
Cardiac	369	29.3	75.9	80.5
CNS	264	26.1	65.2	75.4
Renal	139	25.9	66.7	72.2
Skeletal	266	27.1	77.8	83.3
Nuchal translucency, cystic hygroma	516	41.5	79.7	97.2