1. Construct Validity of a Task-Oriented Bimanual and Unimanual Strength Measurement in Children With Unilateral Cerebral Palsy
Mellanie Geijen, Eugene Rameckers, Caroline Bastiaenen, Andrew Gordon, Rob Smeets


Objective: The purposes of this study was to (1) Investigate aspects of construct validity of peak force measurements of crat- and pitcher tasks using the Task-oriented Arm-hAnd Capacity (TAAC), an instrument designed to measure task-oriented arm and hand strength for cross-sectional and evaluation purposes, and (2) compare TAAC measurements to those of comparative measures using COSMIN guidelines. Methods: In this cross-sectional validity study, participants were 105 children (mean age = 12 y 10 mo; number of boys = 66) diagnosed with UCP. Ten a priori hypotheses were formulated with peak force of the TAAC as index measure and compared to measures on body functions and structure and activity level of the International Classification of Functioning, Disability & Health for Children and Youth (ICF-CY). Strength and direction of the relationship between the TAAC and comparative measures were investigated by calculating Pearson correlation coefficients (r). Results: On body functions and structures level, low- to moderate positive correlations (0.493 to 0.687) were found. On activity level, low negative and positive correlations (−0.271 to 0.387) were found. Conclusion: The construct of peak force measurement of the TAAC is in line with the a priori hypotheses with comparators on body function and structures and activity level, indicating a partial overlap of the construct of the TAAC with both ICF levels. The TAAC appears to be valuable, as it measures functional strength that differs from the constructs of the comparators. More research with a larger population and more comparators is needed. Impact: Clinically relevant information is lacking about the use of strength and strength measurement during daily activities in children with unilateral cerebral palsy (UCP). This study shows that the TAAC provides unique information about functional strength in children with UCP.

PMID: 32936866

2. What is the effect of constraint-induced movement therapy on children with unilateral cerebral palsy? A Cochrane Review summary with commentary
Elena Ilieva, Aleksandra Ilieva


PMID: 32920825

3. Selective Dorsal Rhizotomy for the Treatment of Spastic Hemiplegic Cerebral Palsy
T S Park, Susan Joh, Deanna M Walter, Nicole L Meyer, Matthew B Dobbs
Background: Selective dorsal rhizotomy (SDR) can remove spasticity in cerebral palsy (CP). Spastic hemiplegia is associated with spasticity in the upper and lower limbs on one side. Only a single report described the outcome of SDR specifically in patients with spastic hemiplegic CP. The effect of SDR on spastic hemiplegia requires further investigation.

Objectives: To analyze the outcomes of motor functions, the quality of life, and satisfaction of patients who received SDR for the treatment of spastic hemiplegia.

Methods: A total of 29 children and 1 adult who received SDR were surveyed. The survey questionnaire asked about demographic information, patient's perception of SDR, functional outcomes, SDR surgical outcomes, pain, braces/orthotics, and post-SDR treatment.

Results: Our study included 30 patients. The age at the time of surgery was 2 to 36 years. The follow-up period ranged from one to six years. Of all parents, 90% of parents reported that SDR benefited their children, and 93% stated that they would recommend the SDR procedure to other families of children with hemiplegic CP. Of all patients, 90% reported improved walking, 63% reported improved sitting, and 87% reported improved balance and posture. In daily life functioning after the SDR, 67% were more independent and confident. Moreover, 33% of patients were pain-free and 43% had reduced pain in their legs and back. In activities of daily living, 93% transferred independently from one position to another. A majority (73%) of patients underwent post-SDR orthopedic surgery for heel cord, hamstring, and adductor contractures. Five patients experienced numbness in the small part of the lower limb after SDR. None reported that the numbness affected their daily activities. One child required surgical repair of the cerebrospinal fluid leak.

Conclusions: In our 29 children and 1 adult with spastic hemiplegia, SDR improved motor function and daily life function. Nearly all parents of children and the one adult felt that SDR was beneficial and that they would recommend surgery to other children with spastic hemiplegia.

PMID: 32923208

4. Minimally Invasive SPML Surgery for Children with Cerebral Palsy: Program Development
Dana L Wild, Caroline W Stegink-Jansen, Christine P Baker, Kelly D Carmichael, David A Yngve


Improvements in surgical and rehabilitation care are critical to lessen the burden of cerebral palsy (CP), the most common cause of severe physical disability in childhood. The selective percutaneous myofascial lengthening (SPML) surgical procedure is a minimally invasive method designed to improve ambulation by lengthening contracted musculoskeletal tissues. Information on surgical procedures, efficacy, and safety of SPML for children with CP is lacking. Phase 1 of our research is a "proof-of-principle" study for multisite SPML to improve functional mobility of children with CP, and Phase 2 assesses safety, reoperation rates, and efficacy over time in subsequent patient series. Phase 1 was a repeated measurement case series study of 17 children (mean age 7.6 years). One physical therapist, blinded to the surgeon's measurements, measured bilateral knee and ankle motion before and after SPML procedures, using video recordings of a standardized gait path. Functional Mobility Scale (FMS) 5, 50, and 500 outcomes were taken pre- and postoperatively and via telephone follow-up. In Phase 2, multisite SPML surgeries were implemented in larger successive cohorts from 2006 to 2017. Complications, reoperation rates, and efficacy were retrospectively analyzed. Phase 1 results showed improvement in the children's knee and ankle motion while ambulating and improved FMS 5, 50, and 500 outcomes postoperatively (mean, 6.3 months). At second follow-up (mean 33.3 months), FMS 500 scores continued improvement, while FMS 5 and FMS 50 scores maintained. During Phase 2, the complication rate was 2.4%, and reoperation rates (including reoperations due to maturation) were between 8% and 13%. Improvements to correct ankle equinus were recorded in 498 cases. In conclusion, in a specialized center, single-event, multilevel SPML surgeries of children with CP safely improved ambulatory knee and ankle angle motion and daily mobility outcomes. Future educational studies of training needs for surgeons new to the approach are needed.

PMID: 32922995

5. In-Home Kicking-Activated Mobile Task to Motivate Selective Motor Control of Infants at High Risk of Cerebral Palsy: A Feasibility Study
Barbara Sargent, Kathryn L Havens, Jessica L Wisnowski, Tai-Wei Wu, Masayoshi Kubo, Linda Fetters

Objective: Children with spastic cerebral palsy (CP) have gait impairments resulting from decreased selective motor control, an inability to move the leg joints independently of one another, relying on excessive flexion or extension coupling across the 3 joints. Infants with white matter injury are at high risk of CP and have decreased selective motor control as early as 1 month corrected age. An in-home kicking-activated mobile task was developed to motivate more selective hip-knee control of infants at high risk of CP. The purposes of this study were to determine the feasibility of the in-home mobile task and to determine whether infants at high risk of CP and infants with typical development (TD) learn the association between their leg movements and mobile activation. Methods: Ten infants at high risk of CP based on neuroimaging and 11 infants with TD participated in this cohort study at 3.5 to 4.5 months corrected age. Each infant participated in the in-home kicking-activated mobile task for 8 to 10 min/d, 5 d/wk, for 6 weeks. Learning was assessed weekly -based on an increase in the time that the infant demonstrated the reinforced leg actions when interacting with the kicking-activated mobile compared to spontaneous kicking. Results: With regard to feasibility, participation averaged 92% for infants at high risk of CP and 99% for infants with TD. With regard to learning, the group at high risk of CP demonstrated learning of the task for 2 of 6 weeks, whereas the group with TD demonstrated learning for all 6 weeks. Conclusions: Infants at high risk of CP demonstrated learning of the kicking-activated mobile task but at a reduced amount compared with infants with TD. Further research is necessary to determine whether the kicking-activated mobile task has potential as an intervention to motivate more selective hip-knee control and improve walking outcomes of infants at high risk of CP. Impact: This study investigated the feasibility of an in-home kicking-activated mobile task, a discovery learning task designed to motivate infants at high risk of CP to engage in the intensive task practice necessary to promote their learning abilities and selective motor control.

PMID: 32936921

6. Crouch gait or flexed-knee gait in cerebral palsy: Is there a difference? A systematic review
R O'Sullivan, A Marron, K Brady


Background: Crouch or flexed-knee gait is one of the most common pathological gait patterns in cerebral palsy (CP). Differences exist in definitions used; the degree of knee flexion, inclusion of hip or ankle position, and timing in the gait cycle. This ambiguity may be responsible for variations in prevalence rates and difficulty comparing data across studies. Research question: What are the kinematic parameters used to define crouch or flexed-knee gait in CP gait? A secondary aim was to examine the quality of data reporting, focusing on the sample characteristics, inclusion/exclusion criteria and the choice of limb included for analysis. Methods: Articles included in this review reported on a specified cohort of adults or children with crouch or flexed-knee gait assessed with 3-dimensional gait analysis. A customised data extraction and quality assessment table was designed specific to the research question. Results: The majority (75%) of included studies used the term crouch gait. Where the pattern was defined, 80% of crouch papers and 94% of flexed-knee gait papers based this solely on knee position. Kinematic parameters were clearly defined when they provided objective values of knee flexion, supported this with rationale and provided a reference point in the gait cycle. Only 22% of crouch papers and 19% of flexed-knee gait papers provided this information. The majority of studies (67% crouch; 90% flexed-knee) specified which limb(s) were included for analysis with the majority including both limbs. Objective values of knee flexion ranged from 8 o to 30 o. Significance: This review highlights that crouch and flexed knee are synonymous and ambiguity exists in the kinematic definition making it difficult to make compare data amongst study cohorts. Future research should provide detailed definitions including the threshold value of knee flexion, how it was derived, the timing in the gait cycle and the limb(s) included in analysis.

PMID: 32927222

7. Validity of accelerometry for predicting physical activity and sedentary time in ambulatory children and young adults with cerebral palsy
Ruirui Xing, Wendy Yajun Huang, Cindy Hui-Ping Sit


Background: Objectives: This study aimed to validate five published ActiGraph (AG) cut-off points for the measurements of physical activity (PA) and sedentary time (ST) in ambulatory children and young adults with cerebral palsy (CP). Additionally, four energy expenditure (EE) prediction equations based on AG counts and activPAL (AP) steps were examined in this
population, using oxygen uptake (VO2) as the criterion. Methods: Four male and six female participants with CP (Gross Motor Function Classification System levels I-III, ages 9-21 years) completed seven activities while simultaneously wearing an AG, AP monitor and indirect calorimetry unit. VO2 was measured on a breath-by-breath basis using the indirect calorimetry and was converted into EE using metabolic equivalents. AG counts were classified as sedentary, light PA (LPA) or moderate-to-vigorous PA (MVPA) using five cut-off points: Puyau, Evenson, Romanzini, Clanchy and Baque. The predicted EE was computed using three AG-based equations (Freedson, Trost and Treuth) and an AP step-based equation. Results: Based on 1920 available data points from the 10 participants, Baque (r = 0.896, κ = 0.773) and Clanchy (r = 0.935, κ = 0.721) AG cut-off points classified PA and ST most accurately. All the equations overestimated EE during sitting activities and underestimated EE during rapid walking. The Freedson, Treuth and AP equations exhibited systematic bias during rapid walking, as their differences from the criterion measure increased progressively with increasing activity intensity. Conclusions: The AG accurately classified PA and ST when the Baque and Clanchy cut-off points were used. However, none of the available AG or AP equations accurately predicted the EE during PA and ST in children and young adults with CP. Further development is needed to ensure that both devices can estimate EE accurately in this population.

PMID: 32922459

8. Fifteen-minute consultation: Approach to investigation and management of childhood dystonia
Eva Bridget Forman, Mary D King, Kathleen M Gorman


Dystonia is a hyperkinetic movement disorder characterised by sustained or intermittent muscle contractions causing abnormal movements, postures or both. Dystonia is a challenging condition to diagnose and treat. Dystonia is often under-recognised in children, particularly in cerebral palsy, and frequently coexists with spasticity. This guide aims to simplify the approach to diagnosis, investigation and treatment of childhood-onset dystonia. The principle of treatment is similar regardless of the underlying aetiology: identification of potential triggers and consideration of both pharmacological and surgical options.

PMID: 32928841

9. A Survey of Pediatric Competencies in Entry-Level Physical Therapy Programs in Australia
Emmah Baque, Taryn Jones, Andrea Bialocerkowski


Purpose: To describe perspectives of pediatric physical therapy clinical facilitators on contemporary curricula for Australian entry-level physical therapy programs. Methods: Physical therapy clinical facilitators completed an online survey based on the Academy of Pediatric Physical Therapy of the APTA essential competencies. Results: Conditions including cerebral palsy, cystic fibrosis, and prematurity were highly rated by most participants to include in an entry-level program. Exercise prescription, goal-directed training, and group-based physical therapy were the highest rated interventions. Outcome measures considered important to include were the Alberta Infant Motor Scale and Goal Attainment Scale. Students should demonstrate knowledge and skills using relevant frameworks and have practical opportunities to interact with children. Conclusion: Pediatric clinical facilitators perceived that theoretical knowledge on frameworks, human development, movement skills, pediatric conditions, exercise prescription, and outcome measurement as well as face-to-face experiences with children are important to include in Australian entry-level physical therapy programs.

PMID: 32925813

10. Intersite reliability of vertebral bone marrow lipidomics-derived lipid composition among children with varying degrees of bone fragility undergoing routine orthopedic surgery
Daniel G Whitney, Andrea I Alford, Maureen J Devlin, Ying Li, Michelle S Caird
Background: Lipidomics, a branch of metabolomics, is an attractive technique to characterize bone marrow lipid composition, which may be associated with skeletal acquisition and homeostasis. However, the reliability of lipidomics-derived lipid composition of the bone marrow is unknown, especially for pediatric populations with bone fragility. The purpose of this study was to evaluate the intersite reliability and standard error of measurement (SEM) of vertebral bone marrow lipid composition at the thoracic (T11/T12) and lumbar (L1/L2) spine determined by targeted lipidomics among children with varying degrees of bone fragility undergoing routine orthopedic surgery. Methods: Children aged between 12 and 19 years of age, with a confirmed diagnosis of adolescent idiopathic scoliosis or neuromuscular scoliosis and cerebral palsy, and undergoing routine posterior spinal fusion surgery at our institution were initially included in this study. Transpedicular vertebral body bone marrow samples were taken from thoracic (T) or lumbar (L) vertebrae. Further inclusion criteria involved having bone marrow extracted from both T11 and T12 (n=24) or L1 and L2 (n=19). Lipid composition was measured using a targeted lipidomics technique and examined as the saturated, monounsaturated, and polyunsaturated index and as individual fatty acids. Relative and absolute test-retest reliability was assessed using the intraclass correlation coefficient (ICC) and SEM. Results: For the T11/T12 analysis: the ICC and SEM were 0.59 and 1.7% for the saturated index, 0.31 and 6.2% for the monounsaturated index, and 0.44 and 6.1% for the polyunsaturated index; the ICC showed a considerable range for individual fatty acids from 0.07 (fatty acid 20:2) to 0.82 (15:0) with 62.1% of the fatty acids having poor reliability (i.e., ICC<0.50). For the L1/L2 analysis: the ICC and SEM were 0.50 and 2.4% for the saturated index, -0.12 and 6.0% for the monounsaturated index, and 0.00 and 4.9% for the polyunsaturated index; the ICC showed a considerable range for individual fatty acids from -0.34 (18:1 n-9) to 0.88 (15:0 and 18:3 n-3) with 79.3% of the fatty acids having poor reliability. Conclusions: The intersite test-retest reliability was poor-to-moderate for index measures and generally poor for individual fatty acids for the thoracic and lumbar spine. At this time, it is not recommended to pool bone marrow adipose tissue across vertebral sites for bone marrow adiposity research or clinical monitoring for pediatric populations with bone fragility.

PMID: 32927104

11. Reliability and validity of pediatric powered mobility outcome measures
Naomi Gefen, Amihai Rigbi, Patrice L Tamar Weiss


Purpose: To determine the intra-rater and inter-rater reliability of the Powered Mobility Program (PMP) and the Israel Ministry of Health Powered Mobility Proficiency Test (PM-PT); to test inter-rater reliability of the Assessment of Learning Powered Mobility (ALP) tool; to determine the convergent validity of these measures for children with physical disabilities. Materials and methods: Participants included 30 children (mean 10 years, 6 months [SD 3 years, 7 months]; range: 6-18 years) with cerebral palsy and other neuromuscular disorders. Participants were non-proficient powered wheelchair drivers. Two blinded raters assessed the driving ability by viewing videos of the participants twice as they drove a pre-designed route at ALYN Hospital, Israel. They were assessed via the PMP, ALP and PM-PT outcome measures. Intra-class correlation coefficients (ICC2,1) were used to test intra-rater and inter-rater reliability and Spearman correlation coefficients were used to assess convergent validity. Results: The PMP intra-rater reliability revealed ICCs2,1 of coefficients were 0.97/0.98 for both raters. For the PM-PT the ICC2,1 was 0.89/0.96 for both raters. The PMP inter-rater reliability ICC2,1 was 0.94/0.87 for the two tests, for the PM-PT the ICC2,1 was 0.91/0.87 for the two tests and for the ALP the ICC2,1 was 0.83. The convergent validity between the PMP and the PM-PT was r =0.96, between the PMP and ALP was r =0.89 and between the PM-PT and ALP was r =0.87. Conclusions: The PMP and PM-PT intra and interrater reliability were good to excellent, the ALP inter-rater reliability was good and the convergent validity between all three measures was good to excellent. Implications for rehabilitation There is evidence of validity and reliability for three tests of powered wheelchair proficiency (PMP, PM-PT and ALP). Children using powered mobility, aged 6-18 years, now have outcome measures with empirical evidence that was previously lacking. When time for assessment is limited, the shorter PM-PT can be used instead of the more comprehensive PMP.

PMID: 32924663

12. Future needs of young people receiving botulinum toxin A in paediatric rehabilitation services of New South Wales: focus on transition
Simon P Paget, Anne de Groot, Kerry Hanns, Heather Burnett, Jane Ho

Young people (YP) with neurological disabilities such as cerebral palsy are increasingly living into adulthood and require healthcare transition for services including botulinum toxin A (BoNT-A). We analysed medical records in the three children's hospitals in New South Wales (NSW) and identified 253 YP who are expected to transition from paediatric to adult BoNT-A services in NSW and Australian Capital Territory during 2018-2023. A substantial proportion of these YP have additional needs that will require paediatric and adult health services to work together to improve their life-long health outcomes.

PMID: 32929823

Virginia Liang, Gena Henderson, Jianhua Wu

Background: Whole-body vibration (WBV) is a relatively new intervention paradigm that could reduce spasticity and improve motor function in children with cerebral palsy (CP). We investigated neuromuscular response to a single session of side-alternating WBV with different amplitudes in children with CP. Methods: Ten children with spastic CP aged 7-17 years at GMFCS level I-III participated in this pilot study. Participants received two sessions of side-alternating WBV with the same frequency (20 Hz) but different amplitudes (low-amplitude: 1 mm and high-amplitude: 2 mm). Each session included six sets of 90 s of WBV and 90 s of rest. Before and after each WBV session, we used (a) the modified Ashworth scale to evaluate the spasticity of the participants' leg muscles, (b) a quiet standing task to analyze center-of-pressure (CoP) pattern and postural control, and (c) overground walking trials to assess spatiotemporal gait parameters and joint range-of-motion (RoM). Results: Both WBV sessions similarly reduced the spasticity of the ankle plantarflexors, improved long-range correlation of CoP profile during standing, and reduced muscle activity of tibialis anterior during walking. The high-amplitude WBV further increased ankle RoM during walking. Conclusions: This study demonstrates that a single session of WBV with either a low or a high amplitude can reduce spasticity, enhance standing posture, and improve gait patterns in children with CP. It suggests that low-amplitude WBV may induce similar neuromuscular response as high-amplitude WBV in children with spastic CP and can provide positive outcomes for those who are not able to tolerate stronger vibration.

PMID: 32920250

14. Early detection of cerebral palsy in high-risk infants: Translation of evidence into practice in an Australian hospital
Arrabella R King, Catherine Machipisa, Francyne Finlayson, Michael C Fahey, Iona Novak, Atul Malhotra

Aim: The early diagnosis of cerebral palsy (CP) allows children timely access to early intervention. In 2018, Monash Children's Hospital established an Early Neurodevelopment Clinic based upon evidence-based guidelines for the early diagnosis of CP in high-risk infants. In this study, we aimed to characterise the infants presenting to the clinic and determine the rate of CP diagnosis. Methods: This study analysed data from infants attending the Early Neurodevelopment Clinic between May 2019 and April 2020. Infants at high-risk for CP attended the clinic at 3 months corrected age. Neuroimaging reports were reviewed, and a Prechtl's General Movement Assessment and Hammersmith Infant Neurological Examination were performed. Infants were diagnosed as having typical development, delayed development, high-risk of CP or CP at the time of clinic attendance and referred on to the appropriate pathway. Results: Ninety-six high-risk infants attended the clinic over the 1 year study period. Sixty-eight (71%) infants were extremely preterm or extremely low birthweight, and 28 (29%) were infants at born at older gestation with evidence of moderate to severe brain injury. Nine (9.6%) infants received a CP diagnosis and 12 (12.5%) were considered high-risk of CP. All infants with CP or high-risk of CP were referred to the Victorian Paediatric Rehabilitation Service. Conclusions: It is feasible to implement the early CP diagnosis guidelines into a high-risk infant follow-up clinic. Implementation of the guidelines allows for early diagnosis of CP and appropriate referral of high-risk infants.

PMID: 32940939
15. The neurodevelopmental spectrum of congenital Zika infection: a scoping review
Alessandra Carvalho, Henrique F Sales, Paloma Ventura, Marina Gnoatto-Medeiros, Carlos Brites, Rita Lucena


Aim: To describe the standardized neurodevelopmental outcomes after the first year of life in children with congenital Zika syndrome (CZS) and those exposed to Zika virus (ZIKV) during fetal life, but without microcephaly at birth. Method: This scoping review included observational studies about the standardized neurodevelopmental outcome in children with CZS or exposed to ZIKV, but without microcephaly, assessed after 12 months of age. The databases searched were MEDLINE/ Pubmed, LILACS, Scielo, Scopus, PsycINFO, CINAHL, and Embase. Risk of bias was assessed with the Joanna Briggs Institute Critical Appraisal Checklists. Results: Seventeen papers were included: 12 focused on children with CZS, four on children born without microcephaly, and one described both. Only one of the studies about CZS reported a child with microcephaly and typical development; the remainder described a severe pattern of global developmental delay and cerebral palsy. The prevalence of epilepsy was 74.6%. In the reports about children born without microcephaly, 6.9% to 8.7% had some domain with a score below -2 SD, and three children developed autism spectrum disorder. Interpretation: CZS is associated with severe global developmental delay and cerebral palsy after 1 year of age. In children born without microcephaly, although most have typical development, some may be at risk for impairments.

PMID: 32931050

16. Assessment of risk factors for cystic periventricular leukomalacia
Tomonori Kurimoto, Satoshi Ibara, Masato Kamitomo, Takuya Tokuhisa, Takatsugu Maeda, Yoshinobu Maeda, Chie Ishihara, Yoshiki Naito, Eiji Hirakawa, Tsuyoshi Yamamoto


Aim: Periventricular leukomalacia (PVL) is an important cause of cerebral palsy in premature infants, and cystic PVL is the most serious form of the disease. The risk factors for cystic PVL in singleton fetuses at a gestational age of <35 weeks are unclear. Methods: This study included 2013 singleton birth infants delivered at a gestational age of <35 weeks in Kagoshima City Hospital between 2006 and 2017. The findings for 30 infants with cystic PVL were compared with those for 63 matched control infants by gestational age and birth weight. Results: The cystic PVL was associated with increased incidence of recurrent late deceleration (L/D) (43.4% vs. 15.9%, P = 0.004) and loss of variability (LOV) (10.0% vs. 0.0%, P = 0.03) in fetal heart rate monitoring and late-onset circulatory dysfunction (LCD) (33.3% vs. 11.1%, P = 0.02). Logistic regression analysis revealed that recurrent L/D (odds ratio [OR] = 3.57, 95% confidence interval [CI]: 1.29-10.15, P = 0.01) and LCD (OR = 3.41, 95% CI: 1.09-11.04, P = 0.03) were risk factors associated with cystic PVL. LOV was not included in the multivariate analysis as there were too few cases in both the cystic PVL and control groups. Conclusion: Recurrent L/D, LOV and LCD are strongly associated with cystic PVL. In cases of fetal acidosis related to recurrent L/D or loss of variability, cystic PVL may occur.

PMID: 32924259

17. Histopathology of the fetal inflammatory response to intra-amniotic pathogens
Carolyn M Salafia, Dawn P Misra


Obstetric endorsement of the utility of placental histologic examination remains infrequent, especially from obstetricians who do not have a placental pathologist as part of their own local clinical care team. Placental pathologic examinations are viewed as useless if they do not provide answers to urgent clinical questions. Increasingly, however, it is appreciated that while placental analysis should be considered with regard to its longer term value; results can assess lifelong risks of a wide range of diseases that have been tied to prenatal exposures (e.g., [1]), including distinguishing sex-specific differences in those risks. (e.g., [2]) This review will focus solely on acute fetal (?) inflammation, more specifically, the fetal neutrophil responses in umbilical cord, chorionic plate vessels and to some degree, the fetal system as a whole. This histologic fetal inflammatory response is often the most readily accessible aspect of "FIRS" piece of FIRS (the fetal inflammatory response syndrome). Some researchers have defined FIRS by a combination of both cytokine (especially IL-6) levels and the histopathologic FIR
(Musilova et al., 2018) [3]. As we and others have noted, many histology based FIR cases, even those associated with neurodevelopmental outcomes such as cerebral palsy, are clinically silent (e.g., [4]). Current clinical diagnostic criteria may have high specificity as they are very good at identifying non-FIR cases. However, that high specificity is coupled with very low specificity, identifying only 10% of FIR (Doty et al., 2018 Jul) [5]. Our aim is to provide a conceptual framework for the readers of the journal to better understand how to answer the following questions: What is a neutrophil and how is it important in FIR? What is the differential diagnosis for histologic FIR? How long has there been FIR? What secondary processes may have been recruited (and when) to contribute to the final pathology and pathophysiology of the given pregnancy?

PMID: 32928678