

assessment. Cerebral palsy and cognitive impairment were studied according to early onset sepsis (EOS) and late onset sepsis (LOS) after adjustment for potential confounding variables using multivariate logistic regression models.

Results In total, 139 (5%) of the 2665 live births included had an EOS alone (without LOS associated), 752 (28%) a LOS alone (without EOS associated) and 64 (2%) EOS and LOS associated. At 5 years, the rate of cerebral palsy was 9% (157/1769) and cognitive impairment 12% (177/1495). Compared with uninfected infants, cerebral palsy was increased in the group of EOS alone (OR = 1.70, 95% CI: 0.84–3.45), in the group of LOS alone (OR = 1.71, 95% CI: 1.14–2.56), and this risk was increased further when EOS and LOS were associated (OR = 2.33, 95% CI: 1.02–5.33). There was no association between neonatal infection and cognitive impairment.

Conclusion Neonatal infections among very preterm infants are associated with an increased risk of cerebral palsy at 5 years of age, particularly when EOS and LOS are cumulative.

207 MATERNAL FATTY ACIDS INTAKE DURING PREGNANCY AND LATER CHILD COGNITIVE DEVELOPMENT IN THE EDEN MOTHER-CHILD COHORT STUDY

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Background and aims Polyunsaturated Fatty Acids (PUFA) are needed for child brain development, especially *n*-3 PUFAs. Prenatal exposure depends on maternal lipids intake during pregnancy. We aimed to investigate associations between maternal PUFAs intake during pregnancy and later child cognitive development.

Methods In 1066 children of the EDEN mother-child cohort, we assessed cognitive development at 3 years with the Ages and Stages Questionnaire (ASQ, score between 0 and 300). Maternal lipids intake during pregnancy was evaluated after delivery, using a food frequency questionnaire and a food-composition table. We investigated associations between PUFAs intake and ASQ score using multiple linear regressions adjusted for centre, child's age, gender and gestational age, maternal tobacco and alcohol consumptions, parental education, siblings, caregivers and preschool attendance.

Results Mean ASQ score was 270.1 (\pm 29.4), *n*-6/*n*-3 ratio in food intake was 10.0 (\pm 2.3) and total *n*-3 PUFAs intake was 0.47% (\pm 0.09) of total energy intake. In crude analyzes, ASQ score was positively associated with each three *n*-3 PUFAs (α -linolenic, eicosapentaenoic and docosapentaenoic acids) and negatively with linoleic acid and *n*-6/*n*-3 ratio. After adjustment, ASQ score remained significantly associated with *n*-6/*n*-3 ratio (β = -1.16; SE=0.37; *P*=0.0015). Association with total *n*-3 PUFAs tended to persist (β =1834; SE=985; *P*=0.063).

Conclusions After adjustment for confounders, especially maternal education, higher *n*-3 PUFAs intake and thus lower *n*-6/*n*-3 ratio in pregnancy food consumption were associated with better cognitive development in early childhood. We observed similar results with prepregnancy lipids intake. Our study suggests a role of prenatal nutrition on childhood cognitive development.

208 MANAGEMENT OF NEWBORNS WITH SUSPECTED OR PROVEN CONGENITAL TOXOPLASMA INFECTION IN THE FIRST TEN DAYS OF LIFE

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Congenital toxoplasmosis is caused by transplacental fetal contamination following maternal primary infection.

Risk of transmission increases with gestational age. Severity is higher when transmission occurs before 20 WG leading to abortion, fetal loss, prematurity or severe fetal damage (particularly neurological). After this period, infection mainly affects the eye.

Since establishment of prenatal screening in Austria and France, toxoplasmosis has declined. Early maternal treatment (spiramycin or pyrimethamine-sulfonamide) has shown a lower incidence of fetal sequelae. Combination of ultrasound follow-up, fetal MRI, real time PCR on amniotic fluid allows antenatal diagnosis of severe forms of CT in which termination of pregnancy are accepted. Only 15% of infected liveborn children have clinical signs.

In countries with high incidence of CT and without national program, prenatal and/or neonatal screening are required to improve medical care and minimize sequelae (chorioretinitis, hydrocephalus...). Low prevalence countries recommend neonatal screening or prevention rules.

In case of prenatal diagnosis, clinical examination, serological tests (detection of specific IgM/IgA confirmed at day 10, comparison of immunologic mother-child profiles), transfontanellar ultrasonography and ocular fundus are performed at birth. In lack of prenatal screening, when children are symptomatic, maternal serology (with avidity test), PCR on placenta, neonatal lumbar puncture and tomography are added. In asymptomatic children, diagnosis will be evoked when complications appear (visual impairment, psychomotor delay, seizures...).

Serological tests should be interpreted cautiously in early or late maternal infection, maternal treatment without amniocentesis. Thus infected children have to be treated early to reduce risk of chorioretinitis.

209 MANAGEMENT OF CHILDREN WITH SUSPECTED OR PROVEN CONGENITAL TOXOPLASMOIS FROM DAY 10 TO THE END OF THEIR FIRST YEAR

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Management from Day 10 to Day 365 has two goals according to the results of the work-up performed at birth, and eventually *in utero*. The first is to start treatment and surveillance in infected newborns and, the second, applying to settings where prenatal screening is performed, is to confirm the absence of infection in newborns who are born from a mother who seroconverted during pregnancy but who show no signs of infection at birth.

When congenital infection is proven the standard attitude in France is to start treatment without delay even newborns with no clinical signs. Treatment relies on a combination of pyrimethamine and sulfonamides but there is no consensus on the type of sulfonamides, on the dosages and rhythm of administration and on the length of treatment, ranging from 3 to 24 months. Children under treatment should be monitored regularly for side effects. The decrease of IgG under treatment is a normal evolution and should not be interpreted as a sign of non-infection. Regular neurological and ophthalmological examinations in the first year of life are also important to detect any signs that would deserve special attention.

In the second case, the absence of clinical and biological signs *in utero* or at birth significantly decreases the probability of infection. Repeated serological tests remain however necessary to fully exclude infection by monitoring the decrease of IgG to undetectable levels. Any neosynthesis of IgG would indicate that the child is infected and warrant starting the same treatment as in infected infants.

210 MANAGEMENT OF PATIENTS WITH CONGENITAL TOXOPLASMA INFECTION FROM 1 TO 18 YEARS OF AGE

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At the age of 1 year congenital toxoplasmosis presents a wide spectrum of clinical signs ranging from patent neurological abnormalities to sub clinical infection. At this age treatment is usually discontinued as only cyst stage of parasites are present on which the currently used drugs are inefficient.

Patients with severe lesion, mainly hydrocephalus associated or not to visual impairment usually born from women who were not screened during pregnancy have to be placed in institution or have to be enrolled in special care programs.

Children treated ante and perinatally displayed a totally different presentation. In this setting gross abnormalities are very rare. In a cohort of 480 congenitally infected newborns we observed 5 hydrocephalus. Retinochoroiditis were observed in 8 cases. Ocular lesions are generally diagnosed later in life either because lesions are peripheral or because they occurred later, even after the age of 10. Occurrences or relapses are usually unpredictable but age (6 and 11 years) or pregnancy appear to be periods of risk.

In such clinical settings congenital toxoplasmosis should be considered as a chronic ophthalmologic disease. Whether these patients should be regularly followed is debatable but for counselling pregnant women who seek for information about the long term outcome in their infants such systematic follow up is the only way for providing unbiased information. In a cohort of congenitally infected adults yearly checked since childhood, visual function and quality of life scored well and majority of participant endorsed long term ophthalmologic follow up.

211 OUTCOME OF CONGENITAL TOXOPLASMA INFECTION IN YOUNG ADULTS

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Background Ocular lesions represent the most frequently encountered clinical manifestation of congenital toxoplasmosis (CT). Thus they may be correlated with disease activity, functional damage and impact on quality of life (QoL).

Patients The Department of Parasitology, Hôpital de la Croix-Rousse, Lyon, France, represents a national reference centre for patients with CT. Beyond a European cohort of 430 children with treated CT, 130 presented retinochoroiditis (OT) during a median follow up period of more 10 years.

Results In our European cohort, OT was present at birth in only 10% of instances, but late manifestation beyond ten years of age has to be expected. After 6 years, 24% will manifest OT, increasing to 30% after ten years. Lesions in both eyes have to be expected in 30% of instances, but no child in our cohort had bilateral visual impairment. Not surprisingly, QoL assessment revealed that treated CT has little effect on the vision related QoL and general well being of the affected individuals. This strongly contrasts to outcomes reported from Southern American cohorts with CT where 80% of the merely untreated neonates show ocular manifestations early in life, 65% present bilateral lesions, and foveal involvement is present in 50%, resulting in significantly lower QoL scores.

Conclusions People with OT in Europe show less severe clinical courses and functional damage resulting in better vision-related QoL than individuals living in Southern America, especially since these

frequently have bilateral lesions and more recurrences. Close clinical follow up is warranted in any case with ocular involvement.

212 MECHANICAL SUPPORT IN PEDIATRICS

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ECMO is the implementation of the cardio-pulmonary bypass machine for prolonged periods of time to sustain systemic perfusion and gas exchange. This is an invaluable tool in the care of children with severe refractory cardio-circulatory and pulmonary failure, preferably in patients with potentially treatable and reversible cardiac disease. Development of the ECMO principles, although still not fully supported by evidence-based data, has allowed to progress from a salvage therapy to a more commonly used treatment to allow time for cardio-pulmonary recovery. Therefore, timely initiation of ECMO may impact prognosis. This has been the driving force followed by some centers that have continually available rapid sequence ECMO programs. Nevertheless, selection of the "appropriate" patients for ECMO remains a challenge, is continuously evolving and very institution-dependent. The principle of starting ECMO after failure of maximal medical therapy may be counterproductive. Decision to initiate ECMO in a cardiac patient, particularly after surgery often follows the instinctive judgment of the team. Literature suggests that early initiation of mechanical support in this patient population has been related to better outcomes and better hospital survival. Tendency to initiate ECMO in the early postoperative period or early throughout decompensation seeks to maintain adequate perfusion, to minimize ongoing myocardial insult and to enhance myocardial recovery. The latter may help create a favorable environment for myocardial recovery. Justification for ECMO initiation ought to be based on the patient's lack of capacity to properly perfuse his tissues; hence the need to identify and use early markers of tissue perfusion anomalies.

213 PREVENTING PREMATURITY: USING HUMAN GENOMICS TO UNDERSTAND BIRTH TIMING

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The composition of the biological clock defining the duration of human pregnancy remains a central question in reproductive biology. Our goal is to understand the molecular signals comprising this biological clock to prevent preterm birth. We have generated and analyzed mice with defects in prostaglandin biosynthesis, prostaglandin catabolism, circadian clock molecules, and oxytocin production in efforts to begin to define the key physiological pathways. These genetic studies in mice reveal essential functions for cyclooxygenase-1-generated prostaglandin F2 alpha for labor onset and the degrading enzyme hydroxyprostaglandin dehydrogenase in the maintenance of pregnancy. While these studies have elucidated the pathway for parturition timing in rodents, the findings have resulted in limited understanding for mechanisms of human parturition. In this presentation, data that genetic factors contribute to human preterm birth will be summarized. We have analyzed DNA from families with recurrent preterm birth and control families without preterm infants through genome-wide association and whole exome sequencing. These efforts have identified potentially interesting new contributors to birth timing from the maternal genome, such as the follicle stimulating hormone receptor gene, novel phospholipase isoforms, and pathways harboring rare, predicted deleterious mutations. New data regarding contributors to birth timing from the fetal genome will also be discussed.