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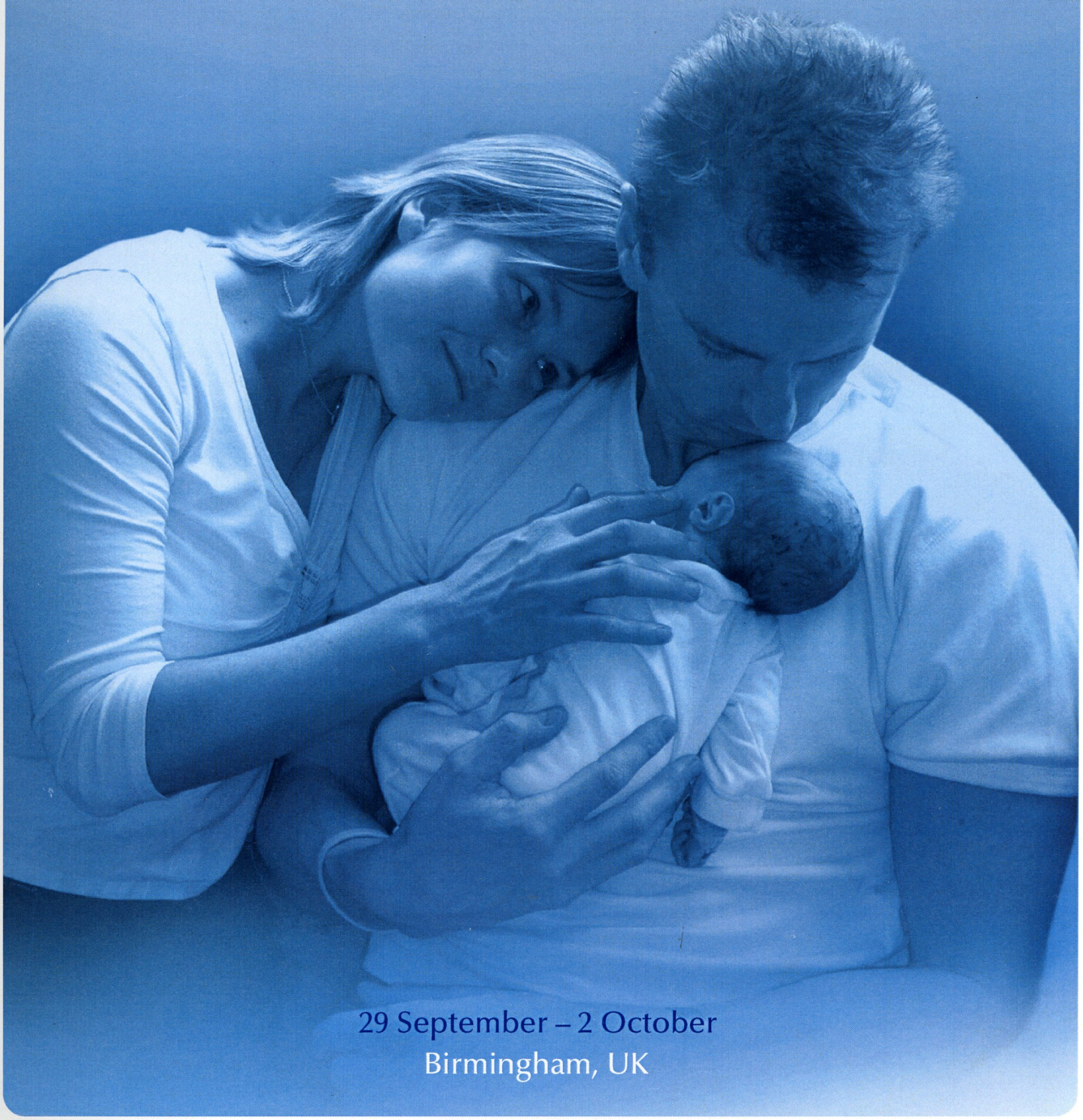
Perinatal Loss: Improving Care and Prevention



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Conference Handbook *Scientific Track*

P48 - Stillbirth versus SIDS: anatomic samples preservation and genetic research

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This project comes under the indications provided by Law n.31 of February 2nd 2006 "Regulation for Diagnostic Post Mortem Investigation in Victims of Sudden Infant Death Syndrome (SIDS) and unexpected fetal death, that stipulates the development of research programmes aimed at reducing unexpected fetal death and Sudden Infant Death Syndrome rates, that are currently a major socio-medical problem.

No in-depth investigations regarding the genetic bases of these pathologies, their incidence and the damaging effect of risk factors are yet present in the literature.

Recent knowledge in the field of molecular genetics suggests a possible involvement of specific genes in the pathogenesis of these syndromes, particularly of SIDS, and the importance of interactions between the genetic constitution and environmental factors in unleashing the fatal effects.

The major obstacle to genetic research is the complex characteristics of the human anatomic samples available. In fact, autoptic biopsies are performed 24 h post-mortem and are usually formalin-fixed. This common fixation procedure, although it is a traditional method of tissue preservation for histopathological examination, compromises the quality and integrity of nucleic acids (DNA and RNA). To solve this problem, in this Institute a novel and innovative buffer, called RNAlater, has been introduced to preserve the nucleic acids: samples treated with this buffer have comparable quality to fresh frozen tissue samples. In this way it is possible to store samples at -20°C indefinitely, without significantly affecting the amount or the integrity of the recoverable nucleic acids.

The main purpose of our study is to expand on molecular genetic research, in order to identify the involvement of specific genes in these syndromes.

In recent studies allelic variations in the promoter region of serotonin transporter (5-HTT) gene have been shown as a novel risk factor for SIDS in American and Japanese cases (Weese-Mayer DE et al. 2003). This gene, located on human chromosome 17q11.2, encodes for a membrane protein that regulates the uptake of serotonin, a neurotransmitter with important roles during embryogenesis and autonomic nervous system differentiation.

The long "L" allele increases effectiveness of the promoter and would lead to reduced serotonin concentrations at nerve endings compared with the short "S" allele.

A new screening protocol of Italian SIDS cases for the 5-HTT gene has been undertaken in our laboratory. The analysis has been extended to SIUD cases and to related controls. The results of the molecular genetic analyses are flanked by macro- and microscopic examinations of other organs and in particular by histological tests on serial sections of the major brainstem nuclei, in order to correlate morpho-functional lesions of the autonomic nervous system with any genetic alterations identified.

P49 - Cardiovascular causes of perinatal loss

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High risk changes in the cardiac action, mostly manifesting with arrhythmias, may be caused by microscopic malformation of the conduction system. The finding of accessory AV communications, particularly nodo-fasciculoventricular Mahaim bundles are rather frequent in perinatal loss as well as in SIDS, but a clinicopathological assessment of their lethal arrhythmogenic potential is often impossible. These congenital abnormalities, under particular conditions and/or neurovegetative stimuli, are liable to provoke electrical inhomogeneity, instability, and desynchronization with impeding risk of malignant junctional arrhythmias. Mahaim fibers have been detected in 39% of sudden perinatal death and in 23% of SIDS victims. These lesions have been attributed to the variable outcome of a "resorptive degeneration" process that normally "reshapes" the junctional pathways in the early postnatal period. Another approach to the same problem can be made by taking into consideration the persistence of ontogenically specialized ring tissue, astride the AV annuli or, as seen in neonatal death victims, putting together a sort of "arrhythmogenic interface" with the ordinary myocardium, at the top of the ventricular septum. Also, the central cardiac structure supporting the conduction system, could possibly interfere with the causation of impulses, as in the cases of cartilaginous metaplasia of the fibrous body, detected in 6% of SIDS and in 19% of sudden perinatal victims. Regarding the long QT syndrome, as a favoring condition for ventricular tachycardia-fibrillation with a high risk of sudden cardiac death, one can say that this thesis is losing ground; the implications of the neurovegetative reflex mechanisms, does not correspond to any clear-cut pathologic changes. Early atherosclerotic lesions of the cerebral and coronary arteries, involving also the sino-atrial and atrio-ventricular arteries, significantly associated with maternal cigarette smoking, are common in the perinatal period. Lastly, cases of fibromuscolar hyperplasia of the pulmonary artery were detected.