

step consists on testing the effects of drugs *in vitro* in cell lines and *in vivo* in mouse xenografts.

To translate the results of this research into the clinical scenario the program includes the development of phase I-II trials. Considering that cancers in children are different from tumours of adults we need to test new drugs in early phase clinical trials specifically designed for children.

In summary, the promotion of early clinical research in children with cancer combined with a better knowledge of the tumour biology will allow a more effective introduction of new targeted therapies into the clinical practice.

Pulmonology

IS-016 ASTHMA DEATHS

R Illes. *Respiratory Paediatrics, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK*

10.1136/archdischild-2014-307384.16

The UK has the highest Paediatric asthma mortality and morbidity in Western Europe. Data will be reported from a longstanding regional (East of England), and the National Review into Asthma Deaths (NRAD). These data clearly describe the risk factors in the UK for asthma death in childhood. Conversely and arguably the UK produces some of the best evidence based clinical guidance (BTS /SIGN, NICE) in the world, however it is clearly failing to deliver quality and safe care to its asthma populations. This contrast has initiated an NHS England quality improvement program; “Delivering improvements in childhood asthma outcomes; A collaborative approach”, to implement a national high impact change model to improve asthma outcomes for children and young people, using the skills, expertise and resources of the 12 NHS England Strategic Clinical Networks. This aims to nationally improve the education of health workers and the asthma population at large, encourage self-management, standardise materials, and review the commissioning of asthma services. Lastly, in a financially challenged health care economy, are such ideals achievable?

Pulmonology Symposium (Supported by and Unrestricted Educational Grant from Chiesi).

Pulmonology Symposium (Supported By and Unrestricted Educational Grant from Chiesi)

IS-017 PULMONARY VASCULAR RESISTANCE IN THE PRETERM INFANT – FROM PHYSIOLOGICAL TO PATHOLOGICAL

N Evans. *Newborn Care, RPA Hospital and University of Sydney, Sydney, Australia*

10.1136/archdischild-2014-307384.17

Serial cardiac ultrasound has given us a window on circulatory transition, both normal and abnormal. Preterm birth is not physiological so physiology has to be assessed in well term babies. Pulmonary blood flow increases with the first breath as resistance falls and these balance each other so that the fall in pulmonary artery pressure (PAP) over the first 4–6 h of life is modest. So, early on, well babies will have PAPs close to systemic pressures confounding early assessment for pulmonary hypertension.

The ‘pulmonary ischaemia’ model of RDS originated from early studies when RDS was a different disease. PAP will fall more slowly in preterm babies ventilated with RDS but, in most

preterm babies, PAP is below systemic BP even in the early hours after birth. Thus the impact is too much blood in the pulmonary circulation due, not pulmonary ischaemia from high vascular resistance and blood bypassing the lungs.

There are exceptions to the above, particularly babies with severe RDS, congenital pneumonia or those born after prolonged oligohydramnios, in whom raised PAP is a consistent finding. Oligohydramnios babies are not common, so have been a difficult group to study systematically but several case series have described this as well as the responsiveness of this group to iNO.

There seems to be sub-clinical persistent raised pulmonary vascular resistance in many babies with chronic lung disease. The significance of this is uncertain but in the most severe cases, pulmonary hypertension can be an important component of the disease.

IS-018 NEW THERAPIES FOR PULMONARY HYPERTENSION AND BPD – FROM BENCH TO BEDSIDE

S Kourembanas, K Sdrimas, CJ Lee, G Hansmann, A Fernandez-Gonzalez, SA Mitsialis. *Division of Newborn Medicine, Boston Children’s Hospital, Boston, USA*

10.1136/archdischild-2014-307384.18

We have used mesenchymal stem cells in preclinical models of pulmonary hypertension (PH) and in the hyperoxia-induced neonatal murine model of bronchopulmonary dysplasia (BPD) to suppress inflammation and improve survival while attenuating alveolar injury and PH. The protective effect was predominantly mediated by paracrine mechanisms, since, cell-free MSC-conditioned media were even more efficacious than MSCs in preventing or reversing established disease. The active moieties that confer the therapeutic efficacy of MSCs remain elusive but likely include secreted proteins, nucleic acids, and membrane components, all potentially packaged in MSC-released microvesicles. We have shown that such particles, a class of which is represented by exosomes, convey the therapeutic efficacy of MSCs in the murine hypoxic model of PH. Exosome treatment was also able to abrogate early hypoxic macrophage influx and downregulate hypoxia-activated inflammatory pathways, thus recapitulating the well-characterised, anti-inflammatory properties of MSCs. The clinical use of MSCs in several on-going trials or the MSC secretome (e.g. exosomes) is a budding new field that represents an exciting and promising approach to therapeutic interventions for diseases of the lung.

The Brain

IS-019 THE EMERGENCE OF CONSCIOUSNESS

H Lagercrantz. *Astrid Lindgren Children’s Hospital, Karolinska Institute, Stockholm, Sweden*

10.1136/archdischild-2014-307384.19

The first breaths of air have since antique time been regarded as the ignition of life as indicated by the word spirits. The newborn becomes animated in this way – i.e. the emergence of consciousness. In modern time a bioethics committee¹ has stated that when the new-born encompasses the capacity to breathe either independently, or with the support of a ventilator is the moral and legal point when human life must be preserved independent of gestational age. Awakening at birth is crucial for being conscious. This is triggered by the stress of being born i.e. mobilisation of catecholamines, cooling due to evaporation of the amniotic fluid