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Conventional mechanical ventilation compared with classic and superimposed high frequency oscillation.

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The gas exchange efficacy of high frequency oscillation superimposed on conventional mechanical ventilation (CMV-HFO) was compared to high frequency oscillation (HFO) and conventional mechanical ventilation (CMV) in the experimental RDS of the rat. Experimental RDS was induced in 36 adult rats by repeated alveolar lavage with saline. Arterial blood gases, tidal volume and compliance were measured before and after 60 minutes of ventilation with pure oxygen. CMV was delivered using a time-cycled ventilator with following settings: P<sub>insp</sub>: 25 mbar, PEEP: 5 mbar, frequency 30/min. The HFO-frequency was 20 Hz, TV<sub>oscill.</sub>: 3.75 ml/kg. With CMV-HFO the ventilator delivered a P<sub>insp</sub>: 15 mbar, no PEEP. The superimposed oscillations had a TV<sub>oscill.</sub> 3.75 ml/kg at 20 Hz. The following results were obtained:

time (min.)	CMV		HFO		CMV-HFO	
	0	60	0	60	0	60
PaO <sub>2</sub> (torr)	73.4	137.3	65.1	76.1	77.9	78.1
PaCO <sub>2</sub> (torr)	73.8	65.0	76.1	57.1	61.5	40.1

Tidal volume increased slightly and equally in the three groups.

Our data do not suggest a beneficial effect of HFO or CMV-HFO in the early treatment of experimental RDS.

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IMPROVED ARTERIAL OXYGENATION BY ALMITRINE IN CYSTIC FIBROSIS ADOLESCENTS. I. Dab\*, C. Melot\*\*, R. Haltermans\*\*, P. Dechamps\*\*, Saint-Pierre

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Chronic hypoxemia following long lasting bronchial obstruction in adolescent C/F is a new problem since improved survival. Serious discomfort as headache, loss of intellectual fitness and even cor pulmonale results. As chronic oxygen therapy is mostly not accepted in mild cases we looked for almitrine, a proven peripheral chemoreceptor agonist, which has been shown efficient in old patients with COPD. It was given to 5 patients with a mean age of 15 years. Before and 20 min after IV almitrine (0.25 mg/kg/h) gazometric, hemodynamic and lung mechanic parameters were measured and the distribution of ventilation-perfusion ratios were determined by the multiple inert gas elimination technique. During almitrine infusion oxygenation (p<sub>a</sub>O<sub>2</sub> varied from 63.0±3.1 to 72.0±2.5 mm Hg, p < 0.02) improved. Alveolar to arterial p<sub>O</sub><sub>2</sub> gradient (from 36.5±3.3 to 30.8±2.4 mmHg, p = 0.10) and venous admixture (from 19.0±3.1 to 13.3±1.6%, p = 0.07) decreased slightly. Pulmonary arterial mean pressure (from 20.3±1.8 to 23.1±1.7, p < 0.01) and pulmonary vascular resistance index (from 254±13 to 300±8 dyne.1 cm<sup>-5</sup>.m<sup>2</sup>, p < 0.02) increased significantly. Minute ventilation (from 8.2±0.7 to 8.1±0.6 l/min, N.S.) did not change. We conclude that almitrine increases arterial oxygenation in C/F by improvement of VA/Q matching. This improvement of gas exchange function of the lung appeared to be related to an increased vascular tone which was well tolerated. These preliminary results deserve to be confirmed by chronic oral treatment.

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RELEVANCE OF MESENCHYMAL THYMUS CELLS (MC) FOR ACCEPTANCE OF ALLOGENEIC MATURE THYMUS GRAFTS AND INDUCTION OF ALLOTOLERANCE IN NUDE MICE  
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Allogeneic thymus (aTh) from an adult immunocompetent donor cannot be transplanted successfully in thymusless nude mice even if the graft is irradiated. The graft is destroyed for unknown reasons and no immunocompetence is achieved in the host. Two approaches were established to achieve acceptance of aTh. In experiment 1, mature aTh was transplanted in nude mice, after specific tolerance to the recipient was induced in the donor during the neonatal period. This resulted in acceptance of the aTh, immunological reconstitution and tolerance to the donor's and recipient's MHC-haplotype as proved by skin-grafts and MLC. In experiment 2, neonatal thymus was grafted into allogeneic nude mice and retransplanted 6 weeks later into nude mice syngeneic to the thymus donor. Before retransplantation, investigation of the thymus tissue by monoclonal antibodies showed predominant MHC-antigen expression of the allogeneic host's haplotype on the intrathymic MCs. Again, acceptance and immunological reconstitution was obtained; tolerance to the MHC-haplotype present on the intrathymic allogeneic MCs was observed. These results demonstrate that mature aTh can be successfully transplanted if "intrathymic" tolerance to the recipient has been induced during the immature status of the thymus. After acceptance of the thymus, tolerance to the donor and recipient MHC-haplotype is achieved, apparently transmitted by the intrathymic MCs. "Intrathymic tolerance induction", therefore, may provide a new approach in the treatment of thymus-deficient patients.

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BRAIN ULTRASONOGRAPHY IN NEWBORNS AND INFANTS.  
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83 babies were followed up by repeated ultrasound studies. 75 were newborns: 34 (1st group) weighed <1500 g (BW 1213±235, GA 31±2.7), 41 (2nd group) weighed >1500 g (BW 2406±735, GA 36±3.4); this 2nd group was studied because of RDS (7), sepsis-meningitis (4), post-asphyxial syndrome (7), myelomeningocele (1), abnormal neurologic patterns (22). 8 (3rd group) were infants studied at the age of 1 to 14 months because of previous neonatal intracerebral hemorrhages (2), meningitis (2), rupture of intracerebral aneurysms (1), macrocephaly (2), myelomeningocele (1). In the 1st group 17 (50%) prematures had major SE-IV hemorrhages. 8 (23.5%) had ventricular dilatation (VD), 1 (2.94%) cerebellar vermis hypoplasia, 1 (2.94%) periventricular leukomalacia. 12 (35.3%) of them died. In the 2nd group 9 (21.9%) had major SE-IV hemorrhages. 1 had VD, 4 (9.75%) cerebral edema, 1 ventriculitis, 1 deviation of the brain axis, 1 periventricular leukomalacia. 3 (7.3%) of them died. In the 3rd group 1 had deviation of the brain axis due to hemiatrophy, 1 VD due to bilateral atrophy, 1 VD associated with myelomeningocele, 1 VD with porencephaly post aneurysmatic rupture. 1 post-meningitis ventricular septation, 1 congenital porencephaly, 1 post-tuberculous meningitis VD, 1 Dandy-Walker syndrome with agenesis of the corpus callosum. The ECHO-Diagnosis was confirmed by CT scan. None of them died. 9 (12%) of the 75 newborns had ventricular dilatation. Ultrasounds are very useful not only for the diagnosis and the follow-up of intracerebral hemorrhages and hydrocephalus in newborns, but they also allow to make other specific diagnosis in newborns and infants.

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Prolonged Indomethacin(I) Therapy in Premature Newborns with Patent Ductus Arteriosus (PDA). Is Drug Monitoring Mandatory?

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It has been suggested, that failure of I induced PDA closure may be related to a low plasma concentration (PC) (1). Thus, it was claimed, that on-line I level monitoring is mandatory for any prolonged therapy (2). 5 boys and 5 girls, mean gestational age 32,3 wks. (28-34), mean birth weight 1430 gms (800-2220) were studied. All had RDS with pulmonary and circulatory congestive failure secondary to PDA. The diagnosis was based on clinical judgement and echocardiography (E). Treatment was initiated according to the following protocol: 0,3 mg/kg of I i.v. 3 x q 12 hrs as loading dose, thereafter 2x 0,15 mg/kg q 24 hrs as maintenance dose (2). I was determined by high pressure liquid chromatography. Furthermore, creatinin-, free water-, osmolar clearance and fractional sodium excretion were determined prior and twice during therapy. Therapy was effective in 9/10 patients. The overall peak I PC was 1,62±0,68 mcg/ml (M±SD) (Range: 0,7-2,8); in 9/10 patients PC after loading dose exceeded 1,0 mcg/ml, maintenance levels were 0,5-1 mcg/ml in 6 patients, 1-2 mcg/ml in 4 patients. In all patients transitory impairment of renal functions occurred, which recovered within 2 wks. No clear dose dependent PC of I was observed. PC of I showed a large scatter in the population studied, but was consistent within each individual. Routine drug monitoring of I for PDA treatment according to the protocol described is not mandatory.

(1) Brash, A. R. et al.: N. Engl. J. Med. 305: 67-72 (1981)

(2) Seyberth, H. W. et al.: Ped. Cardiol. 4 (Suppl. II) 81-84 (1983)

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Establishment of some microflora associated biochemical characteristics of feces during the first years of life. B.S. LINDBLAD, K.E. NORIN\*, B.E. GUSTAFSSON\* and T. MIDTVEDT\* From the departments of Paediatrics and Germfree Research, Karolinska Institute, Stockholm, Sweden. This paper presents a new approach to the study of the colonization of the digestive tract after birth. We have followed the development of four s.c. microflora-associated characteristics\*, MACs to create a basis for later investigations into the impact of diarrheal diseases and antibiotic therapy. The following biochemical characteristics were studied in feces from 53 children of 0-61 months of age: conversion of cholesterol to coprostanol and bilirubin to urobilins, inactivation of trypsin and breakdown of mucin. Our investigation indicates the establishment of microorganisms able to convert bilirubin to urobilins within the second year of life. The mucin degrading and cholesterol converting microbes are established in most of the children during the same period. Tryptic activity was found to be absent in meconium, present in feces from all children up to 21 months of age and absent in half the children at 46-61 months of age and adults. This study indicates that the establishment of MACs in the digestive tract is a remarkably long drawn out process.