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Abstracts for the 1987 Annual Meeting, September 6–10, Padova, Italy

1 MEMBRANE FLUIDITY: A NEW BIOPHYSICAL METHOD FOR STUDIES OF DRUG EFFECTS IN HUMAN FIBROBLASTS. H. Toplak A. Hermetter(++), U. Honegger(+) and U. Wiesmann, Depts. of Pediatrics and Pharmacology(+), Univ. Bern, Switzerland, Dept. of Biochemistry TU Graz, Austria (++).

Effects of the psychotropic model drug desipramine (DMI) on apparent membrane fluidity were measured in suspensions of cultured human fibroblasts in Hank's balanced salt solution by a fluorescence polarization technique using anthroyloxy-stearic acids (AS) as probes. Cells were incubated with 1 uM 6 or 12-AS in prescence or absence of 5 uM DMI at temperatures variing between 37° and 4°C. Fluidity increased with the depth of the probes in the membrane (12 AS > 6 AS) and with increasing temperature. Measured anisotropy r(G), inversely correlated to fluidity, at 37°C in drug treated cells (±SD) was 0.073±0.007 for 12 AS (controls: 0.096±0.012) and 0.124±0.006 for 6 AS (0.130±0.014). At 25°C r(G) was 0.112±0.012 for 12 AS (0.118±0.014) and 0.188±0.011 for 6 AS (0.178±0.008). This suggests that the drug is fluidizing the deeper, hydrophobic layer of the membrane at 37°C, but not at 25°C. Measurements of membrane fluidity in various depth of the membranes may be helpful to study effects of lipid soluble drugs.

2 **Prostaglandin E 2 (PGE 2) Levels in the Lung Lavage Fluid of Premature Newborns Before and After Ductal Closure.** Vogel M, Strasser Th*, Roos R, Riegel K; von Hauner Childrens Hospital and *Medical Clinic Innenstadt University of Muenchen, W.-Germany

The purpose of our study was to provide evidence for a role of PGE 2 in maintaining ductal patency As measurements of plasma PGEs in the literature did not correlate well with ductal patency we examined the tracheal aspirate for PGE 2 by a radioimmunoassay
a) in 7 premature newborns (NB) of a mean 28 (26-30) weeks gestation with a mean weight of 880 (710-1180) grams before and within 24 hours after surgical duct closure performed at a mean age of 12 (7-30) days and
b) in 2 NB of 27 weeks and 850 grams with ductal closure by indomethacin. In those 2 duct closure was confirmed by cross sectional and Doppler echo criteria.
The PGE 2 levels ranged from 240 - 3770 pg/ml (mean=1555; median 880) before duct ligation and fell significantly (p= 0.01) to 0 - 300 (mean 72, median 35) after duct ligation. The wide range of PGE 2 levels before duct closure may be explained by the fact, that 2 NB had been treated with bovine surfactant.
The fact, that PGE 2 in the tracheal aspirate disappear or are markedly reduced after surgical or pharmacological duct closure may be due to cessation of local PGE synthesis in the duct tissue itself.

3 THEOPHYLLINE THERAPY MONITORING USING 24 H SALIVA THEOPHYLLINE CONCENTRATION PROFILES IN AMBULATORY ASTHMATICS. Tal A, Aviram M, Ben-Zvi Z, Gorodischer R. Division of Pediatrics, Soroka Medical Center, Ben-Gurion University, Beer-Sheva, Israel.

We have shown an excellent correlation between plasma (P) and citric acid-stimulated saliva (Sal) theophylline concentrations (TC) (mean+/-SD PTC: Sal TC = 1.78+/-Ø.22, Ped Res. 20:1047, 1986; Pediatrics, in press).
We applied Sal TC determinations for T therapy monitoring by performing 93 Sal TC 24 h profiles in 59 ambulatory asthmatics (mean +/-SD age 8.3+/-3.2 ys) treated with slow release preparations (SR): 5-7 saliva samples were collected by parents at home during a 24 h period. Actual vs estimated PTC confirmed a possible mean error of only Ø.83 mcg/ml in these children. Sal TC were satisfactory in 40 children; therapeutic levels were achieved in 18 (30.5%) only after changing daily dose or dosing intervals; marked morning vs nighttime variation existed in both peak and trough Sal TC ($p < Ø.Ø5$) in 13 children. Highest Sal TC in a 24 h Period was in morning samples in 86%, while lowest level was in evening samples in 84% of the children.
Conclusions: 1. Sal TC is extremely valuable in ambulatory asthmatics. 2. Routine 24 h peak level should be taken 3-4 after morning, and trough level before evening doses of SR.

4 Opiate activity and intestinal transepithelial passage of β-casomorphin (β-CMs) in vitro. D. Tomé, A.M. Dumontier, M. Hautefeuille, J.F. Desjeux. INSERM U.290, Hôpital Saint-Lazare, Paris, France.
The opioid peptides β CMs are derived from milk β-casein in the intestinal lumen. Natural β CMs as well as the analog β[DAla 2,4, Tyr 5]CM5-NH2 caused a naloxone reversible reduction in short-circuit current (Isc) when added to the blood side of the isolated stripped rabbit ileum, in Ussing chamber. After addition in the mucosal reservoir at the concentration of 10-4 or 10-3 M, the natural βCMs did not alter Isc. HPLC analysis of peptides and aminoacids revealed that they were hydrolysed in the mucosal reservoir and that they did not cross intact the tissue. In contrast, the analog, at the same concentration, remained active on Isc ; it was not hydrolysed and it was transported intact across the tissue (Jms = 3.5 ± nmole/hr cm^2 at 10-3 M). Furthermore, the protected analog collected in the serosal reservoir after crossing the tissue displayed an intact aminoacid composition and was active on Isc. These results indicate that βCMs are opiate agonists acting on electrolyte transport. Their action from the luminal side seems to depend on the transfer of the intact peptides from the luminal to the blood side where opiate receptors are located. This action is prevented by mucosal hydrolysis of natural peptides.