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A080

Low cholesterol as a risk factor for medical intensive care patients

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Background: Low cholesterol was previously described as a risk factor in cardiothoracic intensive care patients and possesses a high prognostic significance in terms of in-hospital mortality. The prognostic impact of cholesterol in medical intensive care patients is as yet unknown. In addition, the usefulness of this parameter in the development of a new risk score, which is only based on laboratory parameters, has to be elucidated.
Study design: Patients were monitored on the medical intensive care unit. Blood samples were drawn daily and cholesterol was analyzed by a LX 20 (Beckman Coulter).
Results: 526 patients were included in this study, 40 of whom died on the intensive care unit. 47 patients deceased on the peripheral ward. The duration of hospitalization varies from hours up to 45 days (mean 4.0±5.1 days). Cholesterol decreased sharply after admission in both the deceased (mean value on admission: 140±54 mg/dL) and the survivors (mean value on admission: 175±52 mg/dL). During the first 12 days after admission the mean cholesterol concentration was significantly ($p<0.05$) lower in the deceased [120±9 mg/dL] as compared to the survivors [155±12 mg/dL].
Conclusion: Cholesterol seems to be a useful parameter in predicting patients outcome during the first twelve days on the medical intensive care unit. The inclusion of this data into a risk score is currently under investigation.

A081

Spheroidal coculture model of hepatic stellate cells (HSCs) and endothelial cells: implications for a proangiogenic role of hepatic stellate cells

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HSCs are pericytes of liver sinusoidal endothelial cells (LSEC) and HSCs may provide a pro-angiogenic environment for tumor metastasis by expressing angiogenic factors. Stabilization of newly sprouted endothelial cells (EC) by smooth muscle cells (SMC) is a prerequisite for vessel maturation. Activated HSCs might be a source for SM-like cells. We examined in vitro activated rat HSCs for expression of early and late SMC markers. RT-PCR, immunostaining and western blot analysis revealed that in vitro activated HSCs express in addition to early markers, also SM myosin heavy chain, calponin and h-caldesmon. We further studied activated HSCs in a 3-dimensional spheroidal coculture system together with LSEC and vascular endothelial cells. Coculture spheroids of HUVEC and SMC differentiate spontaneously and organize into a core of SMC and a surface layer of EC representing an inside-outside model of the physiological assembly of blood vessels. Replacing SMC by in vitro differentiated HSCs resulted in a similar organized spheroid with differentiated, von Willebrand factor-producing, the surface lining HUVEC and a core of HSCs. Interestingly, only HSCs in direct contact with the endothelial cells express SMC markers. In an in vitro angiogenesis assay, in vitro differentiated HSCs induce quiescence in EC in a similar way as SMC. In contrast to vascular EC, LSEC spheroids embedded in collagen gels do not form capillary-like structures when stimulated with FGFs or VEGF, but when co-cultured as spheroids with HSCs, LSEC and HSCs organized in the same way as SMC-EC and formed sprouts. Furthermore, sprouting LSEC started to express the vascular endothelial cell maker VE-cadherin. Taken together, in vitro differentiated HSCs appear to be able to adapt a functional SMC phenotype and to form together with LSEC tubular sprouts. Since in liver metastasis, the majority of neoangiogenesis originated from LSEC, the spheroidal coculture model would offer the possibility to adapt new strategies to block forming of new vessels.

A082

Neurotransmitter lithium

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Li-salts are useful in preventing migraine attacks and shortening manic periods by modulating 5HT and NE. Li-treated bipolar subjects show lowered brain to serum conc in ^{7}Li NMR: Li disturbes H-bridges, the electric conductivity, slows down oscillations involved in memory and thinking, in thermoregulation. Li injections into the frog skin gives rise to electrical oscillations.
Li decreases NE transmission, NE release, inhibits basal and beta adrenoceptor-dependent adenylate cyclase, modulats the phosphatidylinositol pathway, interacts with AcCh/ligand-binding and its induced flux, modulats ligand- and voltage-gated ion channels, substitutes for Na and/or H: distributes rapidly to liver and kidney, enters cells via Na channels, incl. K/H_2O-pump (F_0F_1-ATPase): extruded by the active cation pump (and e—driven K,Na/H-exchange-system) at about 1/10 the rate of sodium: accumulates therefore in cells and modulates cellular volume. It interferes with cation binding, with membrane fluidity by interfering with pls/lipids. nAcChR and K/H_2O-Pump were similar in many aspects.
Li inhibits Na/K-ATPase, gives rise to hypertension by induction of (erythrocyte) Na/Li countertransport, Li/Na-exchange-activity; results in hyperthyrodism (inhibition of jodine uptake), in progressive chronic nephropathy, in hyperthermia.
Secondary effects of Li were its anti-inflammatory activity, its immunostimulating and antimirobial properties: its potentiation or suppression of immunity, its possession of pro- and anticancer properties. Li is found to be essential and seems to be a neurotransmitter and/or regulator of their action.
The side effects of Li includes fatique. Above 2 mEq/L more severe toxic signs may occur. The toxicity of Li is increased by factors that deplete the body of sodium. Restriction of dietary sodium dramatically increases the renal reabsorption of Li and can lead to severe toxicity. Similarly, diuretics that lead to Na loss may augment Li toxicity: kidney damage, chronic allergic reactions.
Li is not metabolized, and elimination is predominantly via filtration in the kidney. Renal impairment results in accumulation of Li, with resulting toxicity.
Kiehl R. BioPerspectives 2005, Wiesbaden, www.rki-i.com.

A083

Determination of frataxin/X25 gene GAA-repeat expansions in patients with type II diabetes requiring high dose insulin treatment

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Friedreich's ataxia (FRDA), the most common; autosomal recessive hereditary ataxia, is caused by a GAA triplet repeat expansion in the first intron of the X25/frataxin gene. 30% of FRDA patients have abnormal glucose tolerance, with about 10% presenting with manifest diabetes; it has also been shown that frataxin deficiency in pancreatic islets causes diabetes due to loss of β cell mass. Recently, it was found that frataxin interacts functionally with mitochondrial electron