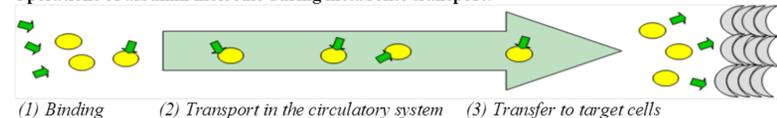


# Detoxifying activity of serum albumin demonstrated diagnostic utility in patients with kidney transplant dysfunction and pregnant women with preeclampsia

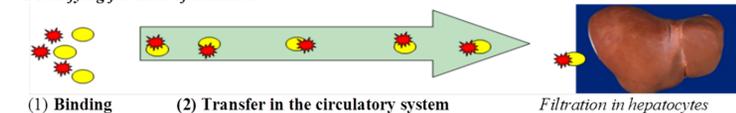
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**Background:** Serum albumin (SA) is an important component of the detoxifying system of the organism. In the circulatory system, SA is the main carrier protein whose detoxifying activity is the binding of hydrophobic toxins and their transport to hepatocytes. The detoxifying activity of SA can be significantly reduced when the SA molecules are overloaded with excessively high level of toxins. This significant reduction in the SA activity leads to an inadequate overall elimination of toxins from the organism. High overall toxin levels cause further deactivating of the SA transport molecules themselves. Such conditions finally result in the escalating intoxication of the patient. We investigated the clinical relevance of the novel, in vitro laboratory test for the detoxifying activity (DTE) of serum albumin, based on Electron Paramagnetic Resonance (EPR) spectroscopy of SA labeled with 16-doxy stearic acid. Recent clinical study of post-surgery patients has already confirmed the clinical utility of the EPR test for prediction and diagnosis of septic intoxication.

## Operations of albumin molecule during metabolite transport:



## Detoxifying function of albumin:



**Objective:** To evaluate the clinical relevance of the EPR test of serum albumin for patients who have a risk for developing intoxications of a non-infective origin.

## The methods and procedures:

We used EPR analyzer AXM-09 (Albutran) and the set of reagents "ATA-test-T" to measure detoxifying activity of albumin in blood samples.

**Investigated samples:** 50 µl of serum or plasma EDTA

### Test procedure:

- (1) venous blood sampling,
- (2) serum separation,
- (3) incubation of a serum sample with the reagent on a shaker for 10 min at 37 °C,
- (4) drawing of the sample into capillary,
- (5) measurement of the sample on AXM-09 Analyzer for 4 min.

**Sample measurement time:** 4 min (15 samples per hour)

## Analytical technique

The ATA-test investigates the serum sample. For that the spin probe 16-doxy stearic acid is added to the sample.

The spin probe molecules are bound specifically on albumin in two basic positions: (1) in the primary binding sites located in the albumin domains I – III (in these sites their mobility is restricted), and (2) in the relatively wide hydrophobic area between the albumin domains in the interior of the protein globule.

Those positions of the spin probe allow comprehensive assessment of the conformation and functional activity of albumin molecule.



## Laboratory electron paramagnetic resonance analyzer "EPR AXM-09"



## Materials:

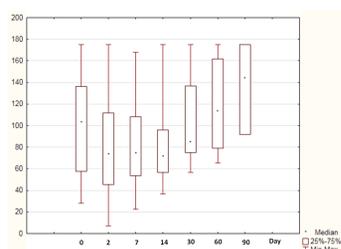
**A)** The observation study included 92 (45 males and 47 females) kidney transplant recipients. 54 of them had the kidney transplant dysfunction such as acute resection (30), ischemia/reperfusion injury (15), nephrotoxicity of calcineurin inhibitors (4) and combination of pathologies (5). The control group included 38 patients, which were observed in early (19/38) and late (19/38) postoperative periods.

**B)** The observation study included 189 pregnant women, including 97 with uncomplicated pregnancy (15-40 weeks) and 92 who suffer from preeclampsia (17-39 weeks).

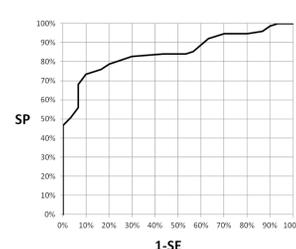
## Results:

**A)** In the patients with kidney transplant dysfunction, there the median value of DTE was found as 55% (34%; 81%) versus 123% (77%; 157%) for the patients of the control group. The diagnostic sensitivity and specificity of the test were 73% and 78%, respectively, for diagnosis of kidney transplant recipients with transplant dysfunction. The cut-off value of DTE was 80%. The ROC-analysis showed AUC of 0.86.

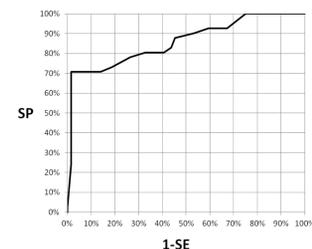
**B)** In the pregnant women with severe preeclampsia, there the mean value of DTE was 57% for second and 42% for third trimesters of pregnancy, versus 82% and 56%, respectively, for women with uncomplicated pregnancy. The diagnostic sensitivity and specificity of the test were 64% and 92% (cut-off of DTE was 52%, AUC=0.79) for diagnosis of severe preeclampsia in second trimester, and 59% and 82%, respectively, in third trimester (cut-off 42%, AUC=0.75).



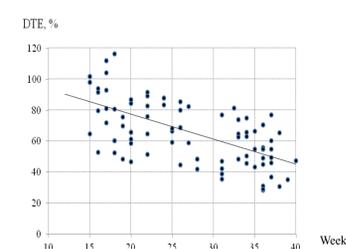
**Fig.1A.** Variation of albumin detoxifying activity in recipients before and after the kidney transplantation



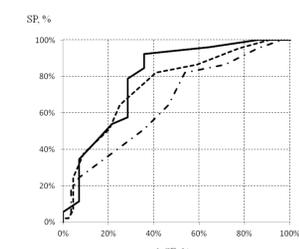
**Fig.2A.** ROC curve for albumin detoxifying activity in recipients with acute resection of kidney transplant



**Fig.2A.** ROC curve for albumin detoxifying activity in patients with dysfunction of kidney transplant



**Fig.1B.** Variation of albumin detoxifying activity in pregnant women during uncomplicated pregnancy



**Fig.2B.** ROC curves for albumin detoxifying activity in pregnant women with preeclampsia:  
solid curve – severe preeclampsia, 2nd trimester  
dashed curve - severe preeclampsia, 3rd trimester  
dash-dot curve – moderate preeclampsia, 3rd trimester

**Conclusion:** The in vitro EPR test of the detoxifying activity of serum albumin is a sensitive and noninvasive method, which clearly has a demonstrated diagnostic utility, for patients with kidney transplant dysfunction as well as for pregnant women with severe preeclampsia. Our results suggest that the detoxifying activity of serum albumin would be applicable as the marker for prediction and diagnosis of escalating intoxications of various origins.