Our research was carried out using a laser flow cytofluorimeter-sorter BD FACSCanto II (Becton Dickinson, USA) with analysis of the obtained results using the FACSDiva 6.1.2 program.

The results. Patients with severe asthma had the lowest levels of ROS in granulocytes compared with the levels in patients with mild and moderate asthma, as well as in the control group (p_{1-3}= 0.0003, p_{2-3}= 0.0017, p to - $_3$ = 0.0150).

Statistical calculation proved a probable decrease in the percentage of dead necrotic granulocytes in patients with severe asthma compared with both the control group and the levels in patients with mild and moderate asthma (p_{1-3} = 0.0009, p $_2$, 0 p k- $_3$ = 0.0177).

There was a direct moderate correlation between levels of 7-AAD positive granulocytes and levels of reactive oxygen species (ROS) in neutrophils (r = 0.5597 p = 0.0006).

Conclusions.

1. A statistically significant decrease in the percentage of dead necrotic granulocytes in patients with a severe form of asthma most likely reflects the presence of a defect in the processes of phagocytosis of neutrophil granulocytes. Violation of phagocytosis leads to deterioration of tissue disposal processes damaged by the chronic inflammatory process and inhibition of recovery processes.

2. The absence of significant differences between the percentage of dead necrotic granulocytes in children with mild and moderate asthma compared with the control group is presumably associated with less inflammation and better lung function.

3. The search for the most sensitive and specific diagnostic marker of the activity of the chronic inflammatory process in asthma continues. Flow cytometry is a modern highly informative method for assessing the morphofunctional state of cells, which allows you to analyze both a population of cells and each cell individually in a versatile way.

4. The introduction of flow cytometry into routine clinical practice for the purpose of early diagnosis of the degree of activity of the chronic inflammatory process would reduce the number of complications and reduce the level of disability.

BIOCHEMICAL MARKERS OF SCHIZOPHRENIA

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Introduction. Identifying biomarkers that can be used as diagnostics or predictors of treatment response (theranostics) in people with schizophrenia (Sz) will be an important step towards being able to provide personalized treatment and would support efforts to develop new drug treatments. Sz is a psychiatric disorder and there have been great efforts to the study of potential neuronal and glial abnormalities that may provide the basis of the aetiology of the disorder. However, findings from such

studies have not yet been translated into biomarkers that are practical in clinical use because brain biopsies are not acceptable and neuroimaging techniques are expensive and the results are inconclusive. Thus, in recent years, there has been search for blood-based biomarkers for Sz as a valid alternative.

Blood-based biomarkers are regarded as a feasible option because the dysregulation of gene expression, epigenetic patterns, protein quantities, metabolic and inflammatory molecules in peripheral blood have been shown to have distinct patterns in people with Sz. In addition, the strong heritability of Sz suggests that there may be genetic markers detectable in peripheral tissue. Finally, there are data that suggest changes in gene expression, epigenetic patterns, proteomic/metabolic markers and functional cellular pathways are present in both the peripheral and central nervous system (CNS) tissue. More recently our concepts about the interactions between the brain and periphery have been expanded with data suggesting that the CNS may influence gene expression and metabolism in the peripheral blood via cytokines, neurotransmitters, or hormones, while immune-related alterations in the CNS may in turn originate from peripheral blood.

Aim of the study. Manuscripts were identified by searching PubMed using the keywords "schizophrenia", "peripheral" and "biomarker", in addition any articles whose title included "schizophrenia" and "peripheral" were also included. The delivery of biological markers for schizophrenia would greatly assist preventative strategies by identifying at-risk individuals who could then be monitored and treated in a manner with a view to minimising subsequent morbidity. This abstract aims to present a selection of biological measures that may indicate risk of schizophrenia.

Materials and methods. A selective and brief review is provided of intensively studied putative markers, including enlarged cerebral ventricles, dopamine D_2 receptor density, amphetamine-stimulated central nervous system dopamine release, plasma homovanillic acid and smooth pursuit eye tracking dysfunction.

Results and discussion. Monoamine neurotransmitters such as dopamine (DA), norepinephrine (NE) or serotonin [5-hydroxytryptamine (5-HT)] have been postulated to associate with pathogenesis of Sz, primarily as a result of the pharmacological profiles of the drugs used to treat the disorder. A number of dopaminergic markers have been evaluated in blood from people with Sz, including DA receptors, DA transporter (DAT), and other molecules associated with the dopaminergic system [i.e., tyrosine hydroxylase (TH)]. Both mRNA expression and receptor binding of DRD2 were increased in lymphocytes from people with Sz who were drug-naive, however the up-regulation of DRD2 mRNA was not replicated. The levels of lymphocyte DRD3 mRNA was reported to be elevated in both people with chronic Sz and people with Sz who were drug-naïve. However, it was also reported to be down-regulated in people with Sz and people with bipolar disorders. For DRD4, the mRNA has been reported to be either down-regulated in CD4 positive T cells or not different in people with Sz. It is noteworthy that higher DRD3 mRNA has been reported in people with heroin addiction, whilst lower DRD4 mRNA has been reported in people with major depression as well as during alcohol and heroin withdrawal.

As well as these changes in markers for DA receptors, DAT mRNA is reported

to be higher in lymphocytes from people with chronic Sz compared to controls, by contrast, reduced DAT binding was reported in people with Sz, suggestive of a lower number of the DAT protein. TH mRNA has been reported as increased in PBMC of both people with Sz and their siblings compared to controls. Other changes such as elevation of plasma homovanillic acid (HVA), a breakdown product of DA, were noted among people with Sz, people in the prodromal phase and those with schizotypal personality disorder but not in people with bipolar disorder, suggesting some disorder specificity. In addition, protein of DA- and cAMP-regulated neuronal phosphoprotein of 32 kDa, a critical downstream target of DRD1 and DRD5-mediated signaling, was decreased in CD4 positive T lymphocytes and CD56 positive natural killer cells from people with Sz in comparison to control group, indicating lymphocytes may therefore function as an easily accessible model to study the DA intracellular signaling in the cells of people with Sz. Overall, some of the markers may prove to be markers for a high risk population, such as people with a family history of the disorder as they were not only dysregulated in people with Sz but also in their siblings as well as in prodromal individuals of Sz or people with schizotypal personality disorder.

One caveat of using monoamine related molecules as biomarkers is that most of the antipsychotics would block their receptors. This effect is not limited to the CNS, therefore the drugs may dynamically change the peripheral profile of monoamine-related receptors and metabolites. Thus monoamine related molecules in the blood may prove to be state markers instead of the stable trait markers that are suitable for diagnosis. However, studies on the longitudinal changes in peripheral monoamine related molecules necessary to address this hypothesis are scarce. Thus, in terms of the effect of antipsychotics, a single study found that lymphocyte DRD2 and platelet 5-HT2A receptor binding were both reduced after treatment with antipsychotics. In addition, lymphocyte DRD3 and DRD5 mRNA was reported to show dynamic, non-linear changes in people with SZ who were drug-naïve in the beginning of follow-up. Briefly, mRNA of the DA receptors peaked at week 2 after taking antipsychotics, after which it decreased but was above baseline at week 8. Finally, it has been reported that both risperidone and clozapine elevate plasma NE levels, with risperidone producing a smaller effect. Logically, considering their close ties with the pharmacological properties of antipsychotics, peripheral monoamine related molecules might be a good indicator for treatment response but current evidence to support this posit is lacking.

Conclusions. Presently, none of these measures has satisfactory performance characteristics in terms of predictive validity, noninvasiveness, ease of testing and low cost that would enable their widespread use. However, a few have potential for further investigation and development.