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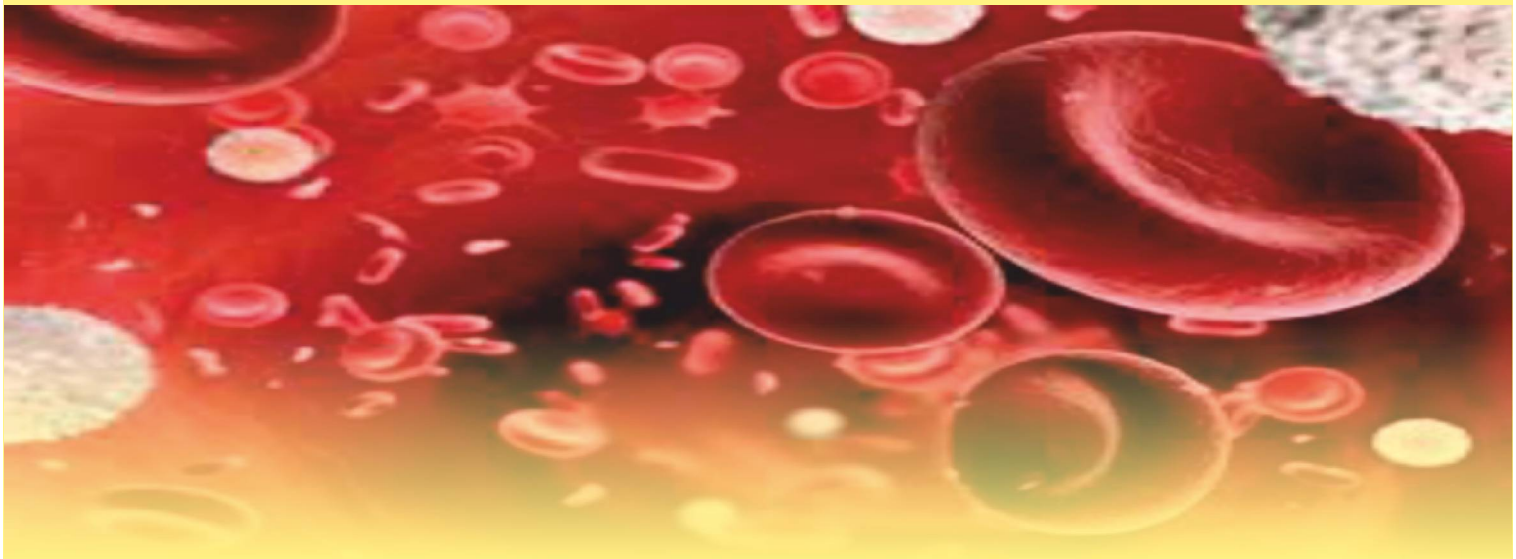
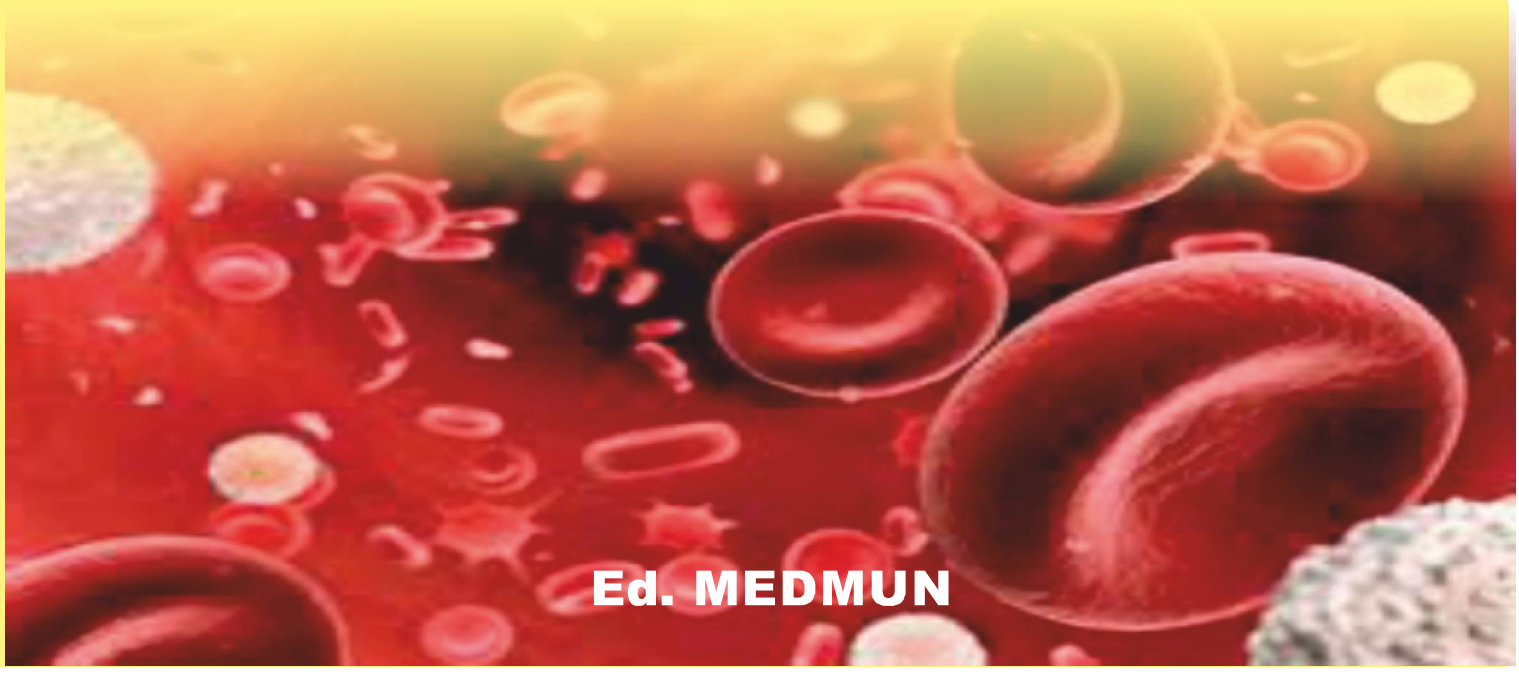


Documenta Haematologica

The Journal of the Romanian Society of Haematology and Romanian National Society of Blood Transfusion

SUPLIMENT Vol.XXXV, Nr. 3-4, 2015



Ed. MEDMUN

Publisher
DE GRUYTER OPEN
Bogumiła Zuga 32A Str.
01-811 Warsaw, Poland
T: +48 22 701 50 15

Address: ***Clinic of Haematology, Fundeni Clinical Institute, 258, Fundeni Road, Sect.2, 022328, Bucharest, Romania***

Subscription: individual 20 RON
institution 50 RON

RSH Account No. RO94RNCB0072049674870001, BCR Sector 1, Bucharest

ISSN - 1582 - 196X **Ed. MEDMUN**

Documenta Haematologica

The Journal of the Romanian Society of Haematology and Romanian National Society of Blood Transfusion

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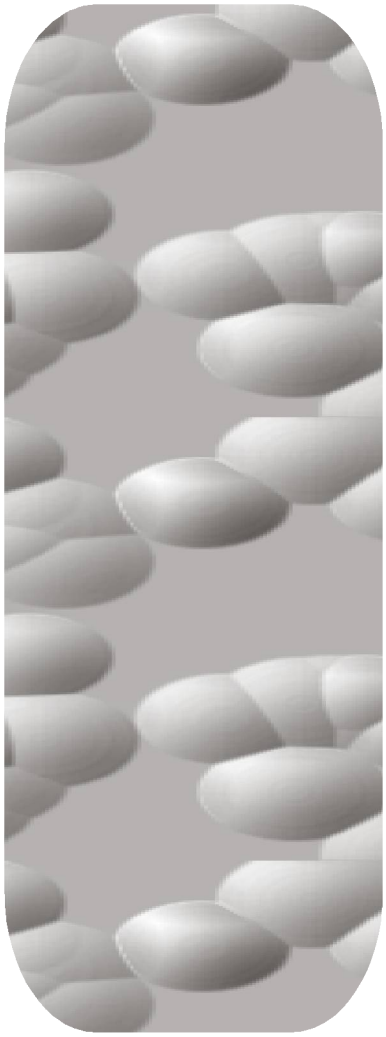
ABSTRACTS Of The XII[th] NATIONAL CONGRESS OF CLINICAL HEMATOLOGY AND MEDICINE TRANSFUSION



NATIONAL SOCIETY OF BLOOD TRANSFUSION FROM ROMANIA

CLINICAL HAEMATOLOGY SECTION
SCIENTIFIC SESSION

EOSINOPHILS AND HYPEREOSINOFILIC SYNDROMES.

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Background

Eosinophils (Eo) are leukocytes resident in mucosal tissues.

While Eo have been considered end-stage cells involved in host protection against parasite infection and immunopathology in hypersensitivity disease, studies changed this perspective. Eosinophils are considered multifunctional leukocytes involved in tissue homeostasis, modulation of adaptive immune responses, and innate immunity to certain microbes. Eosinophils are specialized granulocytic effector cells that produce and store diverse biologically active molecules, including cytotoxic, cytostimulatory proteins, lipid mediators, chemotactic peptides and cytokines[1,2]. Eosinophils can invade target organs after transendothelial migration and secrete their products into the surrounding tissue, thereby triggering local inflammation and tissue remodeling [1-3].

When tissue and/or blood eosinophilia is marked and persistent, the term hypereosinophilia (HE) is appropriate,and Eo derived substances may induce alterations in the microenvironment and chronic organ damage [1,3]. The signs and symptoms associated with Eo may be present, and tissue inflammation is accompanied by local (extracellular) deposition of Eo-derived proteins [3,4], tissue fibrosis and/or thrombosis [3,4].

Hypereosinofilic syndromes (HES) will be defined as blood HE (AEC of ≥1.5 x 109/L) and clinical manifestations attributable to eosinophilia or tissue HE with blood eosinophilia. Blood and/or tissue HE is detectable in inflammatory reactions, certain hematologic malignancies and sometimes in patients with solid tumors [5,6]. Reactive eosinophilia is found in patients with helminth infections, toxic or allergic drug reactions and atopic disorders.

Hematopoietic malignancies accompanied by Eo are:myeloproliferative neoplasms (MPN), variants of acute myeloid leukemia (AML), a subset of patients with myelodysplastic syndromes (MDS), some MDS/MPN overlap disorders, several (T-cell-derived) lymphoproliferative disorders, (advanced) systemic mastocytosis (SM) [1,7-9].

In patients with myeloid or stem cell-derived neoplasms, Eo belong to the malignant clone and fusion genes involving PDGFRA, PDGFRB, FGFR1 or other tyrosine kinases may be present. In chronic eosinophilic leukemia (CEL), the FIP1L1-PDGFRA fusion gene is detected in 10–20% of all cases, and is the most frequent recurrent aberration in CEL.

Definition and classification of HE'HE-related organ damage (hypereosinophilic syndromes)

The normal Eo count in the peripheral blood ranges from 50 to 500 × 10^9/l. Blood eosinophilia can be divided into mild eosinophilia (up to 1500 × 10^9/l) and marked eosinophilia (>1500 × 10^9/l). The term HE should be used when marked blood eosinophilia is persistent, with or without a tissue eosinophilia [10,11]. The Eo are observed in the BM, in lymphatic organs and in the mucosal linings of the gastrointestinal tract (GI) (the stomach, small intestine and colon) [12]. True tissue HE is characterized by a local marked increase in Eo and/or marked deposition of Eo-derived proteins such as major basic protein (MBP) [12]–HES should be divided into variants based on the underlying etiology [13]: idiopathic HES or HEUS (unknown etiology), primary (neoplastic) HES with an underlying clonal myeloid or stem cell disorder , secondary (reactive) HES where an underlying non-neoplastic or paraneoplastic condition is detected and is responsible for the expansion of nonclonal Eo, the lymphoid variant of HES (HE), where the lymphocytes show an aberrant phenotype (CD3−/CD4+).

The patients with unexplained HE, asymptomatic at presentation, may not develop clinical manifestations for many years. These patients would be classified as HEUS, no underlying disease and no organ damage is detected but may develop signs and symptoms of Eo-induced organ damage in the follow up. In HES, organ damage is restricted to certain organ systems: the heart, lungs, skin, spleen, GI tract and central nervous system [14,15].

Endomyocardial fibrosis, development of intracavitary thrombi and occurrence of intravascular thrombosis represent serious cardiovascular complications of HE [16,17]. Endomyocardial fibrosis and thrombus formation are seen in (untreated) patients with eosinophilic leukemias carrying the FIP1L1-PDGFRA fusion gene. These patients respond well to imatinib wich prevents irreversible organ damage.

Clinical HE/HES variants

HES will be divided into 6 clinical variants: myeloproliferative HE/HES (M-HE/M-HES), lymphocytic variant HE/HES (L-HE/L-HES), overlap HES, associated HE/HES, familial HE/HES,

idiopathic HES or HEUS.

Eosinophil-associated diseases are a group of disorders characterized by an increase in circulating or tissue eosinophils.

Eosinophilic gastrointestinal disorders include: eosinophilic esophagitis, eosinophilic gastroenteritis, eosinophilic colitis.

The cardiopulmonary spectrum of EADs comprises: simple pulmonary eosinophilia, acute and chronic eosinophilic pneumonia, Churg-Strauss syndrome, allergic bronchopulmonary aspergillosis, bronchocentric granulomatosis, parasitic infections, idiopathic hypereosinophilic syndrome.

There are hematological malignancies where eosinophilia is reactive (Hodgkin's lymphoma, certain peripheral T-cell lymphomas (PTCLs) derived from CD4 cells, including Sezary syndrome (SS), adult T-cell leukemia/lymphoma (ATLL), and angioimmunoblastic T-cell lymphoma (AITL), are associated with increased reactive eosinophilopoiesis. Hypereosinophilia (HE) may occur in acute B-cell lymphoblastic leukemia, with a substantial impact on disease course[1,6].

Approach to the patient with HE and staging investigations

A detailed medical history should be elicited from all patients with HE, including complete drug/medication and travel histories. Testing for potential helminth infections should be guided by the exposure history.

Nonessential drugs should be discontinued, and the chronology of events between exposure and the development of HE should be determined for the remaining medications. If no drug or infection is identified, a thorough investigation for allergic/atopic or autoimmune disorders, blood cell disorders and other neoplastic conditions should be initiated [18,19].

Important initial parameters include: a complete blood count with differential counts (and microscopy), routine chemistries (tests of hepatic and renal function), levels of inflammatory markers and autoantibodies, serum IgE, vitamin B12 and tryptase levels, molecular test for FIP1L1-PDGFRA.

BM investigation is warranted in all patients in whom HE remains unexplained or a hematopoietic neoplasm is suspected. BM investigations should also include a core biopsy with histology and immunohistochemistry. An immunohistochemical marker panel: CD34, CD117, tryptase and CD25 should be applied [20].

The cytogenetics, FISH and molecular analyses (seeking PDGFRA-, PDGFRB and FGFR1 fusion genes, BCR-ABL, JAK2 V617F, KIT D816V and clonal TcR rearrangement) should be performed [10,13].

The lymphocyte (T cell) phenotyping should be performed in patients with HE to identify aberrant populations, associated with eosinophilopoietic cytokine production [21].

The extent of Eo-mediated organ damage should be assessed: a physical examination with thorough skin examination, detailed cardiologic evaluations: the serum troponins,and echocardiogram (or MRI) , assessment of pulmonary function, chest x-ray, abdominal imaging, gastrointestinal examinations.

Management and therapy of patients with HE and HE-related disorders

- In patients with HEUS and HEF, is important to follow-up the patient without treatment provided that there are no signs or symptoms of Eo-related organ damage despite careful medical monitoring. Both must be regarded as provisional diagnoses, since in both conditions, organ damage may develop over time, or a hematologic or other 'underlying disease may be detected.

The reactive form of HE is best managed by treating the underlying disease symptomatic therapy. If the underlying disease is accompanied by HES and cannot be managed with or is resistant to conventional (symptomatic) therapy, the Eo count can be suppressed with glucocorticosteroids [19,22-24].

When life-threatening manifestations are present or imminent high-dose corticosteroid therapy should be initiated immediately, ranges from 1 mg/kg prednisone to 1 g methylprednisolone depending on the severity of the clinical manifestations. Intravenous dosing should be considered to ensure adequate absorption in patients who have signs or symptoms of gastrointestinal involvement. If the Eo count and symptoms do not improve after 1 to 2 days of high-dose corticosteroid therapy, a second agent should be added.

Imatinib is considered standard firstline therapy in patients with FIP1L1/PDGFRA+ eosinophilia [23-25] with a standard start dose of 100 mg daily or less, some patients require a dose of 400 mg daily [24,26]. In patients who progress to acute leukemia, high-dose chemotherapy and hematopoietic stem cell transplantation must be considered. In patients with FGFR1 mutants, imatinib is not effective, chemotherapy plus allogeneic stem cell transplantation or novel alternative targeted drugs [24,27,28] are potential treatment options. Because systemic corticosteroids remain the first-line therapy for most forms of HES, identification of patients with :(1) secondary eosinophilia requiring specific therapy directed at the underlying etiology (associated HES), (2) PDGFRA-positive MPN or other steroid-resistant eosinophilic myeloproliferative disorders, (3) overlap syndromes that can be managed with topical corticosteroid therapy should be a priority.

The distinction between L-HES, idiopathic HES, and systemic forms of overlap HES becomes an important factor to consider in the choice of second-line therapies when steroid resistance or intolerance develops.

Conclusions:

- Eosinophils represent a distinct hematopoietic cell lineage with unique features. Chronic (hyper)eosinophilia may be accompanied by a characteristic pattern of organ damage.
- Hypereosinophilia (HE) is an important checkpoint in the diagnostic algorithm.
- Independent of the underlying disease, HE-associated organ damage is called hypereosinophilic syndrome (HES).
- In patients with HE, it is important to document or exclude an underlying neoplastic or non-neoplastic disease and the presence of definitive or imminent HE-related organ damage (HES).
- Close clinical follow-up of HEUS is necessary to monitor for development of HES and/or an underlying disease.
- Treatment of HES depends on the underlying disease
- Complete staging of all organ systems, including the skin, lung, heart, BM and blood and GI tract, is essential in the evaluation of all patients with unexplained HE.
- Patients with myeloid or stem cell neoplasms and eosinophila caused by abnormalities in PDGFRA or PDGFRB should be treated with imatinib.

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HUMAN MICROBIOME AND ITS IMPLICATIONS IN HEMATOLOGY.

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Microbiome represents the aggregate of all microbial species on and in the human body. Humans and their microbiome have co-evolved as a physiologic community. The microorganisms living in association with the human body are collectively called the **microbiota**, with most microbe-host interactions being symbiotic as opposed to pathogenic The microbiota can colonize various anatomical sites throughout the human body and contribute to our overall health through physiologic and metabolic processes necessary for survival. Microbiome is the associated genom of the microbiota and it codes for the necessary processes that are not encoded by the human genome. From birth, commensal microbiota prime our immune system to prepare for the millions of immunologic insults we encounter throughout our lives. Microbiota have been transmitted from mother to infant in the birth canal and by breastfeeding. Microbiota acquired early in life are responsible for these functions and remain relatively stable for most of our lives. The microbiota is also dynamic; the abundance or functions of certain species within a community can shift or change in response to typical exposures such as: infection, antibiotics, and/or diet. Food and drug intake impacts the diversity of microbes present.

There are 10 to 100 trillion microbes in a human; microbial cells and particles thus outnumber human cells at a ratio of 10:1. Microbes reside in and on many of the body's sites: the skin and mucous membranes, nares, oropharynx, external ear canal, external eye (lids, conjunctiva), upper respiratory tract, external genitalia, vagina, and intestine. The majority of human-associated microbes reside within the colon, and this microbial consortium is established within the first 3 years of life. Of these lower intestinal microbes, the great majority of the bacteria are phyla: Bacteroidetes and Firmicutes. Each body site has its own microbial community. The human microbiota form an ecosystem. In some cases these sites propagate disbyosis and dysfunction of microbiota which contribute to disease.

Some functions of helpful bacteria to human immune system are: they train our immune system to recognize and destroy pathogens, especially in early childhood; decrease carcinogenic activity; protect against harmful bacteria; produce some antibiotics; reduce respiratory infections, like the common cold. The complex interplay between host genetics and environmental factors is critical in establishing and shaping the microbiota. A healthy microbial community is essential. Dysbiosis, or an imbalance in microbiota composition, is postulated to be a major factor in a variety of human diseases (diabetes, IBD, obesity, cancer). Disbyosis of the gut microbiota can lead to a chronic inflammatory response and cancer progression.

There is a role for the microbiota in normal hematopoiesis. The composition of the gastrointestinal microbiota impacts normal hematopoiesis and can be

involved in hematological disease pathogenesis. The size of the bone marrow myeloid cell pool correlates strongly with the complexity of the intestinal microbiota. Intestinal lymph nodes, Peyer patches, and intestinal lymphoid follicles, only fully develop after birth when they undergo a programmed population change to cope with the microbiota and maintain homeostasis. **Alterations in the microbiota, as well as in specific microbes, are associated with hematologic disorders**. In some cases, pathogens are believed to trigger hematologic disorders; in others, disruption of homeostasis in the microbiota is associated with clinically significant outcomes in patients with hematologic disorders. Microbial organisms have been demonstrated, in some way, to impact every compartment of the hematopoietic system.

There is an important relationship between red blood cells and the microbiota. **Aplastic anemia** has been reported after infections with human parvovirus B19, hepatitis viruses A, B, C, E, and G, CMV, EBV, transfusion transmitted virus, and non–A-E hepatitis viruses. Cyanocobalamin (vitamin B12) is synthesized by several genes of intestinal bacteria. **In anemia of chronic inflammation**, inflammatory cytokines induce hepcidin expression and alter iron homeostasis. Hepcidin is induced by infection and inflammation. Hepcidin-dependent changes in iron flux can induce anemia in chronic inflammatory states. Iron has a role in mediating gut microbiota homeostasis.

Lymphocytes play a key role in responding to microbial colonization by initiating an immune response leading to tolerance or activation. Microbiota are essential for **the development of the mucosal immune system** and plays a role in protection against infectious pathogens. Maturation of intestinal cryptopatches and isolated lymphoid follicles, both considered gut-associated lymphoid tissue, is dependent on the microbiota after birth. A few phyla of bacteria have been specifically implicated in mucosal tolerance via iTreg induction. The microbiota can also directly affect the differentiation of effector T cells. Retinoic acid, which is produced by intestinal dendritic cells, leads to an increased differentiation of Tregs and decreased differentiation of inflammatory Th17 cells. Microbiota have a role in intestinal B cell activation and IgA production. Intestinal IgA can be produced at multiple sites, such as Peyer's patches, isolated lymphoid follicles, lamina propria and mesenteric lymph nodes. The immune system co-evolved with the microbial community to attain a well-balanced symbiotic relationship. Immune system cells respond to microbes following their recognition, by **pattern-recognition receptors**, of microbial-associated molecular patterns expressed on microbes but not on host cells. Host immune cells reside in the lamina propria of the intestine, below the epithelial layer. The crosstalk between resident microbiota and immune cells of the lamina propria is key to maintaining homeostasis in the intestine.

Microbiota can directly **initiate lymphomagenesis**. Microbiota can alter immune parameters to affect lymphomagenesis. Gut microbes can affect the immune system which may impact lymphoma development. Bacteria such as H. pylori, *Campylobacter jejuni, Borrelia bergdorferi*, and *Chlamidia psitacci* play a role in lymphoma development. Many lymphomas are associated with the presence of specific microorganisms: EBV (endemic Burkitt lymphoma and posttransplantation lymphoproliferative disorders), HCV (marginal zone lymphomas), H. pylori (lymphoma of gastric MALT type) , HTLV-1 (adult T-cell leukemia/lymphoma), and HIV. **In acute leukemia**, oral manifestations indicate aberrations in oral microbiota characterized by reduced diversity and abundance alterations, possibly involved in systemic infections, indicating the importance of immune status in shaping the structure of oral microbiome. Any inflammatory process, such as bacterial infection or sepsis, that elevates serum interleukin levels (especially IL-6) may increase the circulating platelet count (**reactive thrombocytosis**). Infections have been associated with **immune thrombocytopenia (ITP)**. There is strong evidence for an association between infection with H pylori and ITP. Platelet concentrations are sensitive to the presence of microbial organisms. CMV, varicela zoster virus and HCV can cause severe **thrombocytopenia**.

The microbiota has impact on treatment outcome. An intact microbiota is required for optimal **response to chemotherapy. In allo-HCT**, the gastrointestinal mucosa is damaged, and colonizing bacteria are impacted, leading to an impaired intestinal microbiota with reduced diversity. The diversity of the intestinal microbiota at engraftment is an independent predictor of mortality in allo-HCT recipients. Interventions to maintain intestinal diversity may lead to improved outcomes in allo-HSCT. Components of the microbiota have a role in the **development of GVHD**. Low gut microbiota diversity post–allo-HCT is associated with the use of systemic antibiotics, and this association is more pronounced in gastrointestinal GVHD.

Intestinal microbiota have systemic effects: are associated with spontaneous arthritis, with the occurrence of diabetes, also affects the amount of energy harvested from the diet and consequentially can play a role in obesity. Gut microbial communities can impact risk for obesity. The gut microbiome associated with obesity might be a biomarker and possibly a therapeutic target. Differences in gut microbial ecology among humans affects the efficiency of their energy

harvest/storage when consuming a given diet.microbiota confer protection against sepsis induced by systemic infection.There is a relationship between intestinal microbiota and the central nervous system. Microbiome may affect human psychology, particularly levels of anxiety, depression and emotion behaviors. Microbiota have a role on anti-tumor immune responses, and a normal microbiota is necessary for responsiveness to anti-tumor therapies. Microbiota have a role on transplant outcomes.

Altering the diet, with its short- and long-term consequences on the microbiota, may have an important impact on maintenance of a poised but controlled immune system and therefore on health. The microbiota co-exist with the host in a unique symbiotic relationship. **The complex crosstalk between the microbiota and the immune system** is critical not only to maintain intestinal homeostasis, but also to prevent systemic pathology.

Tools and approaches to modify the microbiota are being developed in the hope of improving health outcomes: from biological therapies such as fecal microbiota transfer (FMT), to modification of the diet, or to personalized and targeted antibiotic therapies. Probiotic bacteria may help control obesity, hypercholesterolemia, and metabolic syndrome. Probiotics and prebiotics can be effective chemoprevention strategies. Microbiota are involved into the basic mechanisms of carcinogenesis and microbiota also become targets for therapeutic intervention. The microbiota is a biomarker of disease, with both diagnostic and prognostic utility.

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TARGETED THERAPY OF ACUTE MYELOID LEUKEMIA (AML).

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Acute leukemia is the hematopoietic malignancy which has risen the most scientific interest.
Chemotherapy was used in the treatment of acute leukemia over the past 50 years, and was based mostly on the biochemistry of the leukemic cell.

Regarding the targeted therapy, much effort is now being focused on kinase inhibitors following the spectacular success of the bcr-abl tyrosine kinase inhibitors in chronic myeloid leukemia and acute lymphoblastic leukemia Ph positive.The tyrosinkinase controlled cell signaling pathways have been elucidated in a large number of studies and some kinases as FLT3, NPM1, Ras/Raf/MAPK, PI3K/AKT/mTor , aurora kinase, etc were identified as therapeutic targets in AML.

PML-RARa is also an important target for the leukemic cells and the treatment based on this mutation has improved the survival rate of patients with acute promyelocytic leukemia.

The leukemia microenvironment, which has an important role in the development of the leukemic cells, is an interesting field for the development of targeted therapy against the stromal cells.
Micro RNAs are also becoming attractive targets due to their regulatory control of many pathways of vital importance for leukemia proliferation and survival.

All genetic and epigenetic alterations in leukemias result in metabolic alterations, so glycolysis, oxidative phosphorylation and fatty acid oxidation are the center of leukemic metabolomics.
An other important research domain in the field of targeted therapy in AML is the specific immunotherapy using NK and T cells.

Today we witness an exponential development of knowledge in the field of cellular and molecular biology, immunology and epigenetic gene regulation of leukemias. The clinical and laboratory invastigators translate this scientific insights into clinical success,

improving the survival in acute leukemia.

PRIMARY IMMUNE THROMBOCYTOPENIA VERSUS REFRACTORY THROMBOCYTOPENIA– CHALLENGE OF DIAGNOSIS AND THERAPUTICAL APPROACH.

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Isolated refractory thrombocytopenia (RT) represents a modality of presentation of myelo-dysplastic syndromes, clonal disorders of stem cell. The diagnostic criteria are scanty and a standardization is needed, because RT may mimic chronic primary immune thrombocytopenia (ITP). Clinical aspects in RT could be the age of onset after 50 years old, a more expressed haemorrhagic syndrome, or association with macrocytic anemia .The examination of bone marrow smear, karyotype abnormalities, studies of gene expression profile, dysplastic features (micromegakaryocytes, mononuclear forms of megakaryocytes nucleus , cytoplasmic vacuolization , macrothrombocytes, macrocytic anemia) and lack of response at usual treatment are important for establish the diagnosis of RT. Lack of these characteristics cannot exclude a RT. The issue reviews date from the literature concerning diagnosis and treatment of RT.

LEUKEMIA AND LYMPHOMA ASSOCIATED GENETIC ABERRATIONS IN HEALTHY INDIVIDUALS.

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Leukemia and lymphoma - associated chromosome rearrangements are important biological markers in the diagnosis, prognosis, treatment and follow-up of hematopoietic malignant disease. The genetic alteration also are important in tumor genesis.

Although particular genetic rearrangements can be indicative of specific leukemia or lymphoma, evidence in recent years has demonstrated that healthy individuals can carry one or several of these genetic alterations.

Transcripts of BCR-ABL p190 and p210 were detected in 74% and 42 % of healthy individuals respectively. MLL-PTD transcripts were detected in 67% of healthy individuals, the MLL-AF4 transcript in 56 %, the AML-ETO in 18 % and PML-RARA in 50 % of healthy individuals. CBFB-MYH11 fusion is a rare genetic alteration in healthy individuals. Two oncogenic activating chromosomal transcription: t(14;18) (q32; q21) and t (8;14) (q29; q21) and one fusion gene t (2; 5) (q23; q35) from lymphomas were detected in healthy individuals.

All living cells utilize intricate DNA repair mechanism to address different types of DNA lesions and preserve genomic integrity. Pluripotent stem cells have specific needs due to their ability of self renewal and different actions into different functional cell types. Human stem cells posses a highly efficient DNA repair network that becomes less efficient upon differentiation. These cells have an anaerobic mechanism which reduces the mitochondria number and the like hood of oxidative stress.

Human tissues are hierarchically organized into lineages consisting of different cell compartments. The stem cells generise to more differentiated progenitors or transit amplifying cells. The end products are the fully differentiated cells that are post mitotic.

Telomere length can bee used to distinguish between mutations originating in progenitors versus stem cells. Telomere length can bee efficiently measured using flow FISH cytometry. If the mutation in originated progenitor cells we expect to see that the telomere length of aberrant cells is significantly shorter. Transient leukemia – lymphoma specific genetic aberration in healthy individuals originate in progenitors with an increased telomere shortening. In contrast the persistent mutation most likely originating in stem cells with less signs of telomere shortening.

Mutations in progenitors will be driven to extinction by the exhaustion of the cellular replicative capacity. These dynamics would seen as a transient mutations in healthy individuals.

ADOPTIVE CELL TRANSFER - A NEW STEP IN TREATING HAEMATOLOGICAL MALIGNANCIES.

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T cells play an essential role in removing from the human body of infected cells and the cells that have undergone malignant transformation. This antitumor effect physiologically exercised by the T lymphocytes is fundamental property that is based on this new form of immunotherapy - adoptive cells transfer (ACT). In fact, allogeneic bone marrow transplantation (alloSCT) is the most effective form of immunotherapy that uses ACT - the T cells from donor recognize and eliminate

malignant cells of the host (graft versus leukemia effect - GVL). T lymphocytes from donor have a dual effect: triggers the reaction of graft versus host disease (GVHD), with often fatal consequences and the GVL response. The first attempts to eliminate the T lymphocytes from the graft to mitigate GVHD, were marked by a high rate of relapse of disease through lack of GVL. An important step in the development of ACT was successful use of donor lymphocyte infusion (DLI) in patients with myeloid malignancies who relapse after alloSCT. DLI is the first successful attempt to get GVL (desired action) with minimal reactivation of GVHD (undesired).

Through genetic engineering it succeeded in transferring of the receptor with high affinity for tumor antigens in T lymphocytes (from host or donor). CAR T-cells represent the model of success - they are autologous T cells bearing receptor chimeric antigen (CAR). This CAR contains four elements: the receptor for recognition of the antigen (fragment of variable region from a monoclonal antibody specific for an antigen), a transmembrane domain (CD8 alpha or CD28), a signaling domain intracellular derived from cell receptor T (chain CD3); and one or more co-stimulatory domains (derived from CD28 and / or 4-1BB / CD137). Depending on the structure of this complex (availability of these four elements) there are three generations of CAR T-cell. This complex receptor, inserted into T cell will allow recognizing, lysis of the tumor cell and eradication of leukemic cells carrying this antigen. The best clinical results are obtained with CAR T cell recognizing cellular antigen B - CD 19 - expressed in acute lymphoblastic leukemia, chronic lymphocytic leukemia and other lymphoproliferative B. The most serious limitations are related to the toxic effects: cytokine release syndrome, encephalopathy and B cell aplasia.

CAR T cells therapy is a new method of immunotherapy that add in the cancer-fighting along with: alloSCT, monoclonal antibodies, tyrosine kinase inhibitors, inhibitors of bcl 2, bispecific antibodies (BITE), immunecheckpoint inhibitors.

Keywords: *lymphoproliferative disease, immuno-therapy, adoptive cell transfer, chimeric antigen receptor*

CHRONIC LYMPHOCYTIC LEUKEMIA – A PERSONALIZED THERAPY MODEL.

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Chronic lymphocytic leukemia (CLL) is the most common leukemia in developed countries considered a disease of the elderly, with peak incidence between 50-70 years, mean age 65 years. Most often indolent disease, often asymptomatic, is caused by clonal expansion of CD19 + CD5 + B cells (B-1 subset). This disease was considered for 40 years an "accumulation" disease and is due to a defect in cell death program, cell immune incompetence, which may occur at a time disease (defined by number of clonal B cells > 5,000 / mmc in peripheral blood and bone marrow infiltration over 30%), passing through an intermediate phase of "monoclonal B lymphocytosis." CLL risk increases progressively with age, and is 2 times higher in men than in women, in some cases described the phenomenon of familial aggregation among grade 1 relatives.

Indication of treatment is defined by the criteria of progression of the disease: significant symptoms B, cytopenias not caused by autoimmune adverse reactions, autoimmune phenomena that do not respond to immunosuppressive therapy, lymphadenopathy, hepatomegaly, splenomegaly with mass effect or stage Rai III-IV / Binet C. At the same time, treatment is tailored patient status, patients 'unfit' benefiting only palliative treatment, while patients "fit" are stratified by genetic and molecular prognosis, primarily by del cr17 and / or mutation p53, which selects the worse prognosis and that indicate treatment with monoclonal antibodies or inhibitors of kinase Bruton, allogeneic stem cell transplantation including but according to the "pattern" of the patient. Being a chronic disease, the risk of relapse is defining and therapies relapse criteria are applied depending on the individual patient, which orients targeted therapies, which makes CLL to become increasingly a personalized therapy model.

CLONALITY, MALIGNITY, CLONAL EVOLUTION IN HEMATOLOGY.

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The pathogenesis of hematological malignancies is originated from the complexity of human hematopoiesis concept and through the mechanism of malignant transformation. Each entity belonging to hematological malignancies, whether part of myeloid or lymphoid neoplasm, it is heterogeneous in term of biological, clinical and prognostic issue. Further more, each neoplasia is unique and heterogeneous in terms of cellular component.

Clonality represents the common point for all of these hematologic diseases (T.E.?), concept that implies a cell population derived from a single cell. The origin of this clone it is considered to be the neoplasic stem cell,

which can either belong to multipotent hematopoietic stem cell compartment, either be a stem cell more or less differentiated with self-replication ability.
The malignant transformation requires a sequence of genetic events with cumulative and non-lethal character, followed by further incidentally genetic/ epigenetic events that complete the malignant transformation. This malignant transformation pattern is edifying in the case of CLL (MBL) and multiple myeloma (MGUS), but things seem similar in other hematological malignancies (SMD, SMPC, AML).
Tumor cell heterogeneity is marked by two aspects: the presence of cell with tumorigenic potential and without clonal evolution phenomenon , which in Darwin pattern may ensure the neoplastic evolution and progression. This phenomenon/(event) it is considered to be necessary in any malignancy, frequently exacerbated by chemotherapy and radiotherapy, in hematology being obvious the appearance of accelerated/ blast phase in CML, the histological transformation of NHL indolent, B-lymphoma, Richter syndrome.
This new issues have major therapeutic implication. The use of chemotherapy with different action mechanism, synergistic or additive, maintaining dose intensity until reaching marrow transplant, all those represent classical principles of curing intent in oncology. Targeted therapy of tumor specific biological pathways in CML represent the limit, new approaches that interfere with multiple biological pathways in neoplasia stem cell will be necessary. Blocking self-replication mechanisms, blocking the interactions between microenvironment and the malignant clone, strategies as synthetic lethal (sequential activation of several genes that lead to cell suicide), immune and genetic manipulation, all are nowadays areas of intense research. Another option of transforming cancer may concern eliminating intense cytoreductive therapies, where is possible, in a chronic disease.

HEMATOFAGOCYTIC SYNDROME IN HEMATOLOGIC MALIGNANCIES.

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Hemophagocytic lymphohistiocytosis (HLH) is a very severe and rare syndrome of uncontrolled, pathologic immune activation characterized by cytopenia and clinical signs and symptoms of extreme inflammation caused by cytokine release, systemic macrophage infiltration and multiple organ failure. In essence, HLH could be defined as a hyperinflammation in the context of an activated yet ineffective immune system.

HLH is designated as primary (familial, genetic) when associated inherited genetic defects affecting genes responsible for encoding molecules that participate in immune mechanisms or secondary (acquired) HLH describing patients with the HLH phenotype in the absence of a known genetic cause. Primary HLH occurs in infants or small children, while secondary HLH affects subjects of any age, typically in the setting of immunodeficiency or an underlying malignant, infectious, or autoimmune disorder.

HLH is related to impaired cytotoxic function and consequently onset of an uncontrolled inflammatory response with the activation and expansion of interferon γ (IFN γ)–producing T cells. High levels of IFN γ lead to macrophage activation and overproduction of proinflammatory cytokines, which can cause severe tissue damage and organ failure.

Hemophagocytic lymphohistiocytosis is diagnosed by a group of signs, symptoms and laboratory abnormalities. Typical clinical findings include hepatosplenomegaly and prolonged fever that is usually unresponsive to antibiotic therapy. Lymphadenopathy, different kinds of rash, edema and jaundice are less frequent manifestations. Laboratory findings include cytopenias, hyperferritinemia, elevated transaminases, hypofibrinogenemia, hypertriglyceridemia, hypoalbuminemia and hyponatremia, elevated soluble IL-2 receptor and reduced natural killer (NK) cell cytotoxicity, signs of disseminated intravascular coagulation. The pathology hallmark of HLH is the phenomenon of hemophagocytosis It is important to note that the diagnosis of HLH does not fundamentally depend on this morphological finding, because hemophagocytosis can be absent in the early stages of the disease.

Adult HLH can complicate the course of various disorders – inefctions (especially EBV), malignancies, autoimmune diseases, transplantation.

Malignancy associated HLH has been reported in patients with lymphomas or leukemias of the T- or NKcell lineages, anaplastic large cell lymphoma, early B-lineage lymphoblastic leukemia, myeloid leukemia, mediastinal germ cell tumors and other solid tumors. In many of these patients, HLH is triggered by bacterial, viral or fungal infection in the context of immune dysfunctionalities caused by chemotherapy for the malignancy or cytokine production by the tumor cells.
Treatment has to be prompt, as HLH is associated with high mortality in the absence of therapy.

Treatment is complex targeting the suppression of the cytokine storm and the inadequate activation and proliferation of cytotoxic T cells and macrophages (corticosteroids, etoposide, IVIg, cyclosporine, stem cell transplantation – in selected cases) as well as intensive support measures, antiinfectious therapy.

MYELOFIBROSIS FROM CLINICAL DATA TO CLINICAL PRACTICE.

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MF is a clonal neoplastic disease characterized by bone marrow fibrosis, splenomegaly, and debilitating symptoms .

MF is life threatening and is associated with shorter survival.

MF may be primary (PMF) or secondary to ET or PV (post-ET/post-PV).

Histological characteristics: Chronic myeloproliferation, Atypical megakaryocytic hyperplasia, Fibrosis of the bone marrow

Laboratory abnormalities: Anemia: most common – Hb < 10 g/dL in ~50% of patients, Leukoerythroblastosis, Leukocytosis or leukopenia, Thrombocytosis or thrombocytopenia, Increased serum level of LDH, Elevated circulating CD34-positive hematopoietic progenitor cells, Low total cholesterol.
Molecular abnormalities: JAK2V617F mutation in ~50% of patients, MPLW515L/K mutation in ~10% to 11% of patients, new (less frequent) JAK-activating mutations being discovered, eg. LNK , Chromosomal abnormalities - del(20q), del(13q), +8, +9

Clinical Issues in Patients With MF : Shortened survival, Increased risk of leukemic transformation, Severe anemia (often requiring frequent RBC transfusions), **Severe thrombocytopenia or neutropenia, Marked hepatosplenomegaly** (early satiety, severe abdominal discomfortchanges in bowel habits, painful splenic infarcts, portal hypertension leading to ascites and variceal bleeding, compromised mobility, cachexia), **Nonhepatosplenic extramedullary hematopoiesis** (cord compression, ascites, pulmonary hypertension, pleural effusion, lymphadenopathy, skin tumors), **Thrombohemorrhagic complications, Leukocytosis or thrombocytosis, Profound constitutional symptoms** [fatigue (prognostic of worse outcome), cachexia (prognostic of worse outcome), pruritus, night sweats (prognostic of worse outcome), low-grade fever, bone and joint pain], **Recurrent gout.**
We are showing our clinical experience regarding patients with myelofibrosis, their particularities, efficacy and safety profile of treatment.

CLINICAL HAEMATOLOGY SECTION
BONE MARROW TRANSPLANTATION SESSION

HAPLOIDENTICAL STEM CELL TRANSPLANTATION – A NEW TYPE OF TRANSPLANT IMPLEMENTED IN FUNDENI CLINICAL INSTITUTE.

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Haploidentical stem cell transplantation (HaploSCT) is an attractive form of transplantation for patients lacking an HLA identical donor, due to the immediate availability, ease of stem cell procurement and the possibility to further collect donor cells for cellular therapy. Historically, HaploSCT has been limited by the high rates of graft rejection and acute graft-versus-host disease (aGVHD), while a strong anti-tumor effect was observed. Recently, administration of high-dose cyclophosphamide early post transplantation, in combination with tacrolimus and mycophenolate mofetil for GVHD prevention, has proven safe, and produced engraftment and GVHD rates similar to HLA-matched sibling transplants.
We are presenting the results of the first 9 procedures of haploSCT at Fundeni Clinical Institute between Jan 2015-Apr 2016.
Seven patients, between 2 and 65 years old, was transplanted with HaploSCT: 2 patients received second haploSCT from the same donor, due to the engraftment failure; 1 patient received haploSCT as second transplant after an engraftment failure from unrelated transplant. Four patients received haploSCT for AML, 1 for MDS, 1 for HL and one for LMMC. The conditioning regimen was Fludarabine-Melphalan (4 pts as first conditioning and 2 patients as second conditioning) and Fludarabine -Busulfan –Cyclophosphamide (3 pts). Bone marrow was the stem cell sourse in 6/7 patiens at first transplant.
Primary engraftment was achieved in 57% (4/7 pts). All the patients (3/3 pts) who not engraft received busulfan conditioning regimen. Secondary engraftment (after second graft from the same donor) was 100 %. Day-100 non-relapse mortality (NRM) was 28 % (2/7 pts). The cumulative incidence of grade II-IV aGVHD was 28% (2/7 pts) and cGVHD 0% . One patient relapsed. Four pts are alive and in CR (between 3 month and 18 months).
These results suggested that HaploSCT can be a safer approach in case of lacking of identical donor. Conditioning containing Busufan can be associated with a increased rate of engraftment failure, as was demonstrated in cord blood transplants.

AUTOLOGOUS STEM CELL TRANSPLANTATION IN HODGKIN'S DISEASE IN ADULTS – EXPERIENCE OF FUNDENI CLINICAL INSTITUTE.

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Autologous stem cell transplantation (ASCT) is , according to recent international guidelines, standard treatment indication in Hodgkin's Disease in chemosensitive relapse and in first line refractory disease that respondes to salvage chemotherapy. For patients who have primary refractory disease or refractory relapse the procedure could be considered as clinical option, due to poor results in clinical trials.

In this paper we are showing the results and experience of Fundeni Clinical Institute with ASCT in Hodgkin's Lymphoma between June 2001-April 2016.

We performed 165 ASCT in patients with ages between 18-63 years old (87 female and 78 men). 25 % (41) of patients were in chemo-refractory disease, 23% (38pts) were in complete remission (≥CR2) si 52% (86 pts) were in partial remission after salvage therapy. Complete remissions at 100 days were in procentage of : 24%, 95% and respectively 60%.
Transplant related mortality was 4,2%

Our results are similar with the dates from medical literature and they show the need to obtain the best response in controlling the disease before ASCT.
The procedure is safe, well standardized, with the best long term results, in case of complete remission (PET-CT negative) before transplant.

ACQUIRED HEMOPHAGOCYTIC SYNDROME FOLLOWING AUTOLOGOUS HEMATOPOIETIC STEM CELLS TRANSPLANT.

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Background. Hemophagocytic lymphohistiocytosis (HLH) is a rare syndrome of pathological immune activation characterized by extreme inflammatory manifestations, occurring either as a familial disorder (familial HLH –FLH) or as an acquired condition (secondary –sHLH) in association with infections, rheumatologic, malignant or metabolic diseases. HLH occurring after stem cell transplantation (SCT) (SCT-HLH) is a very rare complication, difficult to diagnose and characterized by severe clinical manifestations and high mortality.

The aim of the study is to present the experience of Colțea Bone Marrow Transplantation Unit with SCT-HLH in patients after autologous SCT (ASCT)

Patients and Method. In the last 30 month we performed 46 ASCT in patients with myeloma and lymphoma. In 3 cases we diagnosed SCT-HLH using the criteria published by Takagi et al. requiring 2 major criteria and 4 minor criteria. The major criteria are (1) engraftment failure, delayed engraftment or secondary engraftment failure after SCT, and (2) histopathological evidence of hemophagocytosis. The four minor criteria are high-grade fever, hepatosplenomegaly, elevated ferritin and elevated serum LDH. Treatment was complex including corticosteroids, etoposide, cyclosporine, IVIG and vincristine.

Results All 3 patients were males with ages ranging from 19 to 57 years, receiving ASCT for various types of lymphoma (1- T/NK cell nasal-type lymphoma, 1-mantle cell lymphoma, 1- Hodgkin's lymphoma). Diagnoses was performed by demonstrating bone marrow hemophagocytosis in association with delayed engraftment and the presence of high ferritin and LDH levels in all cases. Genetic testing was not performed. In 1 patient (57 years) the most striking clinical manifestation was confusional syndrome in the absence of IRM visible cerebral lesions. There was no evidence of infection in either of cases. In all cases, SCT-HLH responded to treatment and all patients are alive after a period of 6-18 months after the resolution of HLH.

Conclusions. In our department we noted a particular high incidence of SCT-HLH especially in the setting of ASCT. Considering the young age of 2 of the patients (19 and 29 years respectively), genetic testing would have been useful. In is notable that therapy associating immunosuppression and chemotherapy with IVIG was successful in all cases with this otherwise very severe complication.

CLINICAL HAEMATOLOGY SECTION
ORAL PRESENTATIONS SESSION

PET-CT IN ASSESSMENT OF FREE-DISEASE INTERVAL IN PATIENTS WITH HODGKIN DISEASE.

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INTRODUCTION: Lymphomas are the most frequent hematological malignant disorders which implies lymph nodes. Hodgkin disease is one of the most frequent malignancies in young population. Early detection of recurrences/residual disease in different intervals after therapy has an essential role in establishing the opportunity and therapeutic attitude.

MATHERIAL AND METHOD: In our presentation we will try to show the role of Fusion Imaging Technique PET-CT, in post-therapy period also long-term follow-up in case of complete remission/suspected recurrence/residual disease. We will present the main actual standard accepted diagnosis criteria (Chesson, Deauville, Lugano). PET-CT scan was performed using a GE Discovery IQ scanner at 60 minutes following iv administration of 2-3,7 MBq/kg of 18F-FDG, with use of contrast agent in all cases excepting allergic antecedents, with a scan range from tentorium to proximal third of thighs.

RESULTS: PET-CT scan was performed at the end of treatment for histological-proven Hodgkin disease and also after various time intervals for end of treatment (which included chemo and radiotherapy in some cases), due to clinical new signs and requests of doctors. Comparison with other imaging techniques (mainly CT with iv contrast agent, MRI) were made when this type of scans was performed with maximum 45 days before PET-CT scan. For our patients, the median follow-up duration between the end of chemotherapy and relapse/ new tracer uptake in residual lesion was calculated.

CONCLUSSIONS: Negative PET-CT study at end of therapy is an predictor of good prognosis, some false-negative results being observed in PET-CT studies performed early after the end of therapy. Diagnostic accuracy of PET-CT in post-therapy period is superior compared with CT with contrast agent.

THE CONTRIBUTION OF HBS1L/MYB rs9376092 SNP TO THE OCCURRENCE OF MYELOPROLIFERATIVE NEOPLASMS – A STUDY ON 678 PATIENTS.

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Introduction
JAK2 46/1 haplotype and TERT (telomerase) rs2736100 SNP (single nucleotide polymorphism) have the most important contribution to the constitutional genetic predisposition for BCR-ABL negative myeloproliferative neoplasms (MPNs) - polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF). Recently, other SNPs

have been described as possible modulators of this genetic predisposition. Here we aimed to assess the contribution of HBS1L/MYB rs9376092 (A>C) SNP to the occurrence of MPNs.

Material and methods

The study included 678 patients. There were 236 patients with PV (all of them JAK2 V617F-mutated), 347 patients with ET (212 JAK2 V617F-mutated, 98 CALR-mutated, 10 MPL-mutated, and 27 triple-negative), and 95 patients with PMF (51 JAK2 V617F-mutated, 28 CALR-mutated, 3 MPL-mutated, and 13 triple-negative). All the patients had a known status for JAK2 46/1 haplotype (the rs10974944 tagging-SNP) and TERT rs2736100, with JAK2 46/1 haplotype strongly associating mainly with JAK2 V617F-mutated MPN, and TERT SNP strongly associating equally with all MPN. The HBS1L/MYB rs9376092 SNP was genotyped by a TaqMan real-time PCR assay. The study also included 429 apparently healthy individuals, serving as the control group.

Results

HBS1L/MYB rs9376092 SNP (AA and AC genotypes) was similarly distributed in controls as in PV, PMF and MPN (as a whole) groups (p-value >>0.05 for all these comparisons). There was a weak correlation between the AA homozygous genotype and ET group as a whole, without reaching the statistical significance (OR = 1.467; 95% CI = 0.904 to 2.401; p-value = 0.16). This trend was seen also when analyzing each ET molecular subgroup (eg. JAK2 V617F or CALR-mutated), the effect being somewhat greater in the case of CALR-mutated ET, but again without reaching statistical significance (OR = 1.668; 95% CI = 0.8275 to 3.399; p-value =0.16). Interestingly, there was an excess of AA homozygous genotype in JAK2 V617F mutated ET compared to JAK2 V617F-mutated PV (OR = 2.654; 95% CI = 1.209 to 5.938; p-value = 0.01). A similar trend was observed when comparing JAK2 V617F mutated PMF with PV, but without reaching statistical significance (OR = 2.428; 95% CI = 0.817 to 6.5; p-value = 0.11).

Conclusions

According to our results, HBS1L/MYB rs9376092 SNP has a very modest contribution to the occurrence of MPN. Among MPN entities, this effect seems to be restricted to ET only.

ADULT ACUTE MEGAKARYOCYTIC LEUKEMIA - CLINICAL AND BIOLOGICAL ASPECTS.

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Acute megakaryoblastic leukemia (AMKL) is a rare form of acute and accounts for 3–5% of all acute myeloid leukemia. Although known as a distinct entity for a very long time, because of lack of distinct clinical features and morphological criteria, it is difficult to diagnose this variant correctly. Nowdays, immunophenotyping represents the gold standard, but it is not available in all the centers.

Our aims were to present the immunophenotyping features of AMKL cases from our department between 2015 and 2016, to compare the immunophenotypes and to corroborate them with clinical, morphological, cytochemical, and immunocytochemical findings from all our cases.

BIPHENOTYPIC ACUTE LEUKEMIA AND GRANULOCYTIC MEDIASTINAL SARCOMA. AGRESIV CYTOSTATIC TREATMENT AND PERIPHERAL STEM CELL ALLOTRANSPLANT.

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Biphenotypic acute leukemia (BAL) is an uncommon clinical entity. It is a type of acute leukemia with features characteristic of both the myeloid and lymphoid lineages and for this reason is designated as mixed-lineage, hybrid or biphenotypic acute leukemia.

The precise incidence among acute leukemia is uncertain, although it is likely to account for approximately less then 5% of all acute leukemia .

Probably it arises from a multipotent progenitor cell

and carries a poor prognosis. Although there are no uniform criteria about whether to treat these patients as ALL or AML, it is likely that an intensive approach with high-dose therapy followed by bone marrow transplantation will be required to eradicate the disease permanently. The features of 100 mixed-phenotype acute leukemias (MPALs), fulfilling WHO 2008 criteria, are documented. It has been included in the WHO classification of haemopoietic malignancies as acute leukaemia of ambiguous lineage.

Myeloid sarcoma is found in 2%-8% of patients with acute myeloid leukemia (AML). Myeloid sarcoma may develop before or concurrently with AML, or may be the initial manifestation of AML relapse in previously treated patients. Myeloid sarcoma is a rare extramedullary solid tumor consisting of immature myeloid cells and most commonly involving the bone, skin, lymph nodes, soft tissue, gastrointestinal tract and testis. Mediastinal myeloid sarcoma is very rare, may precede leukemic stage for months or years, and which is frequently misdiagnosed, mostly as malignant lymphoma.

We report the case of 21 years old patient/ young woman, diagnosed with cardiac tamponade, mediastinal myeloid sarcoma and acute biphenotypic leukemia that required reduction surgery and aggressive chemo-therapy for survival.

Key words: Biphenotypic acute leukemia, mediastinal myeloid sarcoma, complex surgical therapy, chemotherapy.

CORRELATIONS BETWEEN IMMUNOPHENOTYPE AND GENETIC ABNORMALITIES IN ACUTE LEUKEMIAS.

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Background. Acute leukemia is a significant challenge for diagnosis and treatment, regarding quick and accurate diagnosis and adapted treatment to prognosis, because of high risk of refractory response to treatment in relapse.
Aim. Our study proposes to identify specific features in acute leukemia by immunophenotyping, in correlations to genetic abnormalities in a group of patients analyzed over a period of two years.
Methods. There were analyzed 160 newly diagnosed patients with acute leukemia. Other features were analyzed: sex, hematological parameters, morphology, immunophenotype, genetic abnormalities by cytogenetic and molecular biology methods. Immunophenotyping and cytogenetic analysis was performed from fresh bone marrow aspirate, and molecular biology from peripheral blood.
Results. Within the cases of acute lymphoblastic leukemia (ALL), 11 of 28 were found with coexpression of KOR-SA and the correlation with presence of Philadelphia chromosome (Ph cr) / BCR/ABL was found in 4 cases. One case was pre-B ALL and 1 were mature B cell ALL, and the others 2 cases were pro-B ALL subtype, 1 with supplementary CBFB-MYH11. Two cases had coexpression of myeloid markers, strong suggested for 11q23 abnormality, and MLL gene, 14 of cases were suggestive for FLT3/ITD mutation because of aberrant CD7 expression, with 2 confirmed cases because of the tardive implementation of method, and 5 cases suggestive for AML1/ETO expression because of association of CD34+ CD56+ CD19+ expression on blasts. Nine from AML cases were suggestive for 11q23 abnormality / MLL gene related with CD56 aberrant expression. Ambiguous acute leukemia cases were not expressed aberrant markers.
Conclusion. Multiparameter analysis by immunophenotyping by flowcytometry of acute leukemia cases was high informative for further genetic abnormalities and is an important tool to discriminate different prognosis subtypes. Quick results by multiparametric flowcytometric immunophenotyping analysis is an important tool to evaluate at diagnosis the prognosis and for therapeutic decision making in acute leukemias.

ACUTE PROMYELOCYTIC LEUKEMIA RELAPSE – THERAPEUTIC OPTIONS.

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Acute promyelocytic leukemia (APL) is a particular subtype of acute myeloid leukemia associated with high early mortality rate. A distinct feature of its clinical course is that almost all the cases who survive to the induction chemotherapy, achieve complete remission (CR). Recently published studies suggest that the complete remission rate is of 90%, while the relapse rate is of 5-20%, out of which 3-5% have extramedullary relapse site. First used in the 90s, the combination of

arsenic trioxide (ATO) with ATRA has emerged as an effective treatment of relapsed acute promyelocytic leukemia. Consequently, this association became the first line indication for low-risk APL patients. Patients treated with combination of ATO and ATRA had significant shorter time till achievement of CR, earlier recovery of platelet counts, decreased PML-RARA transcripts, and less relapses. In high-risk patients chemotherapy is required complementary to combination of ATO and ATRA. Some of the prognostic factors for relapse are late CR achievement (after 35 days of ATRA) are older age, cellular prognostic markers like CD56, CD34.

There are no current standard guidelines for treating patients with APL after relapsing. Treatment with ATO, ATRA, tamobarotene, GO and/or chemotherapy and autologous/allogeneic hematopoietic cell transplant, are the only therapeutic options available for relapsed APL.

Herein we report 5 case of patients with first relapsed acute promyelocytic leukemia, age 20 to 63 years-old. Before relapsing, 4 patients were identified as low-risk (Sanz score), while only one of them was high-risk. All patients received initial treatment according to AIDA and APL protocol. After relapsing, 2 patients were treated with combination of ATO and ATRA and they obtain molecular remission One patient received AIDA regimen for induction and then consolidation cycle containing ATO and ATRA, and 2 patients were treated with ATRA and chemotherapy, but only one survived and achieved molecular remission.

ATO is not approved in Romania, reason why patients with APL and relapsed APL receive conventional chemotherapy. If complete remission is obtained after conventional therapy, patients can be further proposed for autologous/allogeneic hematopoietic cell transplant.

IMPACT OF FISH EXAMINATION ON THE PROGNOSIS OF PATIENTS WITH MULTIPLE MYELOMA: A SINGLE CENTER EXPERIENCE.

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Multiple myeloma is a very heterogeneous disease with indolent evolution for some patients, but evolution aggressive for another category of patients. Therapeutic strategy is adapted to risk: no treatment in patients with indolent disease; complex treatment (proteasome inhibitors, immunomodulatory therapy, chemotherapy, autologous bone marrow transplantation) in patients with aggressive disease. Risk stratification systems are dynamic according with therapeutic advances. Very used for risk stratification is the International Staging System (ISS) which establishes three prognostic groups (stage I, II, III) depending on the level of albumin and beta 2 microglobulin. Recent studies have shown that risk stratification based on FISH and cytogenetics is useful in choosing a risk adapted therapy. Patients with hyperdiploid, t(6;14) and t(11;14) have the best results in terms of survival with the current treatment approach being considered standard risk. Patients with del 17p, t(14;16) and t(14;20) have a poor prognosis and these changes indicate a high risk disease. Patients with hypoploid, t(4;14) or del13 indicates an medium risk. Recently, experts try a combination of the International Staging System (ISS) and risk stratification system based on FISH (presence of t(4;14) and del17p as unfavorable risk markers).

Starting with 2012 we have succeeded, in our Cytogenetic Laboratory from our Center, to implement FISH examination for the patients diagnosed with multiple myeloma. Until this moment we have analyzed 52 patients based on high-risk cytogenetics : del 17p, t(4;14), t(14;16).

We have followed the clinical status , treatment response, progression free survival and overall survival. Our results are similar to those from other related studies .

Conclusion: FISH examination / cytogenetics is an essential tool in the management of patients with multiple myeloma and should be implemented in all hematology centers that treat such patients.

This work was supported by the grant CEEX 74/2006 from the Romanian Ministry of Research and Technology.

A RETROSPECTIVE ANALYSIS OF ATLL CASES BASED ON A 5-YEAR MULTI-INSTITUTIONAL EXPERIENCE.

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Objective: To analyze all the cases of ATLL for the past 5 years in four Hematology centers in Bucharest and to determine the mean survival rates taking into account the ATLL subtype and chemotherapy.

Methods: Records from eighty eight patients diagnosed with ATLL were studied from 2010 to 2015 from the fallowing Hematology centers in Bucharest: Fundeni Clinical Institute, Bucharest Emergency Teaching Hospital, Coltea Hospital and Colentina Hospital. The patients were classified according to the Shimoyama classification in acute, lymphoma, chronic and smoldering ATLL. The mean survival rates were calculated using standard statistics methods.

Results: There was a slight female predominance in our population (F 49, M 39, ratio F/M 1.25) with a mean age of 49.2 years ± 13.9 (F 48.9 years ± 14.9; M 49.7 years ±12,6). According to Shimoyama classification there were: 47 (54%) patients with acute type ATLL, lymphoma type 37 patients (42%), chronic type 1 patient (1%) and smoldering type 3 patients (3%). The majority of patients were treated using CHOP/CHOEP chemotherapy ,50 patients (56.8%), LSG15 chemotherapy ,12 patients (13.6%) or other types of chemotherapy , 26 de patients (29.5%). Only 17 patients received at any given time antiretroviral therapy consisting of interferon or interferon and zidovudine. The mean overall survival was only of 5 months for aggressive forms (acute and lymphoma type) and there were no gender differences regarding survival.

Conclusion: This analysis shows a slight female predominance in our ATLL population, 49 patients (55%). The majority of cases were aggressive type ATLL with acute type ATLL being the most common, 47 patients (54%). The overall mean survival rates were similar, 5 months, for the aggressive type ATLL and there was no survival advantage seen in any chemotherapy regimen used.

THE UEHB EXPREINCE IN MOLECULAR DIAGNOSIS OF ACUTE LEUKEMIA – IMPLEMENTATION OF FUSION GENE SCREENING & FLT3-ITD DETERMINATION.

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Introduction. Acute leukemia (AL) is a clonal disorder of hematopoietic cells characterized by a complex molecular landscape with a high rate relapse post-treatment. The most common form of AL in adults is acut e myeloblastic leukemia (AML) aproximately 80%, the other 20% being represented acute lymphoblastic leukemia (ALL). For these disorders there are available molecular tests for diagnosis, prognosis, and to monitor treatment response. The standard medical conduct, firmly established internationally, is problematic to implement in Romania because of limited financial resources, human resources and logistics. Considering these constraints, we implemented at the UEHB a work flow for fusion gene screening and FLT3-ITD, which we currently describe.

Materials and Methods . Total RNA was extracted for whole blood of bone marrow samples collected on EDTA or PAXgene tubes by manual (RNAEasy, Qiagen) or automated (QIASymphony, PAX Gene total RNA, Qiagen) methods, as per the producer's instructions. The lineage diagnosis was made by immunophenotyping by flow cytometry. For the screening of recurrent fusion genes: in AML we used a panel of 3 tests – CBFB-MYH11, RUNX1-RUNX1T1, şi PML-RARA; in ALL we used a panel of 3 tests – E2A-PBX, MLL-AF4, BCR-ABL1. We used a 2-step PCR with a first revers transcription step, followed by individual amplification, in duplicate, of each fusion gene mentioned. Inconclusive and positive results were reanalyzed using commercial real-time PCR kits (Ipsogen Screening Kits, Qiagen). For FLT3-

ITD determination, genomic DNA from whole blood or bone marrow collected on EDTA was extracted using the automated method described, or by manual protocol. PCR product length analyses was made with the Bioanalyser system and DNA 1000 kit (Agilent). For each reaction (fusion genes and FLT3-ITD) the presence of fragments with the predicted length +/- 10% was verified by microcapillary electrophoresis. Control samples for the process were used, as per the standardized methods.

Results. There were 67 screening tests made for patients with suspicion of AL (58 AML si 9 ALL). In patients diagnosed with AML we identified: 3 with CBFB-MYH11, 3 with AML-ETO, 3 with PML-RARA. In patients diagnosed with ALL we identified 3 positive for BCR-ABL1, of which 1 patient also associted the CBFB-MYH11 fusion gene. The rate of inconclusive tests was lower using the PAXgene tubes and automated extraction method. FLT3-ITD determination was made in 29 patients, of which 2 were positive.

Conclusions. We succeeded in establishing a diagnostic work-flow process for patients with acute leukemia, process which respects quality criteria and has similar performances with commercially available diagnostic kits.

CLINICAL HAEMATOLOGY SECTION
PEDIATRIC HEMATOLOGY SESSION

HEREDITARY THROMBOPHYLIA.

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Hereditary thrombophylias are quite rare diseases, but they could have a severe vital impact (eg. fulminans neonatal purpura, DVT/pulmonary thromboembolic disease, cerebral sinus thrombosis, pregnancy and puerperial complications,etc). Family history plays an important role in diagnosis. Clinical suspicion starts from recognizing unprovoked DVT/PTE in young persons, recurrent thrombosis without an underlying cause, thrombosis in unaccustomed locations or from some specific complications of pregnancy and puerperium.

The laboratory diagnosis is based on complex, specific tests, available only in highly specialized and accredited laboratories, but we have to be careful to random variations and to the difficulties of interpretation.

The screening has to be done only in peculiar patients, aiming that the results could lead to a specific therapy (eg. therapy of acute thrombotic episode, primary and secondary prophylaxis of DVT/PTE. use of contraceptive drugs, etc)

The therapy is based on specific measures in specialized pediatric Hematology-Oncology Centers with adequate equipments and experienced staff.

KEY WORDS:children amd adolescents,venous and arterial thrombosis, hereditary thrombophylia, prophylaxis and treatment:

OUTCOME OF CHILDREN WITH ALL IN ROMANIA. A 10-YEARS MULTICENTRIC ANALYSIS.

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Introduction. The ALL-BFM trials were designed to optimize the treatment of children and adolescents with acute lymphoblastic leukemia (ALL) by reducing treatment-related toxicity by in patients with standard risk features and also by increasing treatment intensity in the subgroup of patient with high-risk features. In the ALLIC-2002 study, event-free survival (EFS) reached 83% for patients in the standard risk group and 75% in those assigned in study the intermediate risk group. **Aim**. To evaluate the diagnostic features, treatment options and treatment outcome of children and adolescents with ALL in Romania, admitted over a period of 10 years in the 10 Romanian pediatric onco-hematology centers. Material and methods. This is a retrospective cohort study performed on a number of 971 patients, consecutively admitted between 2003-2012 in the Romanian centers. The patients were divided based on the period of admittance: cohort 1 between 2003-2007 and cohort 2 between 2008-2012.

Patients older than 18 years at diagnosis were excluded from the study. Male-female ratio was 1.4 and median age at diagnosis was 5 years. Statistical analysis was performed using IBM SPSS Statistics software, version 19, 2010 SPSS, Inc. For the survival analysis we used the Kaplan Meier method and comparisons were made by log-rank test. Results. Preliminary results show that the percentage of patients with a leukocyte count over 10e5/μL at diagnosis was 16.18% and 75% of the patients were FAB-L1. Immunophenotyping could be performed in 84.66% of the patients, the majority of the investigated patients. Molecular analysis, in terms of detection of gene rearrangements, could be undertaken for only a small percentage of the patients, TEL-AML1 (ETV6/RUNX1) being present in 10.21% of the analyzed patients. 10 years-EFS was 75.8% for those belonging to cohort 2 and over 69.3 % for cohort 1. **Conclusions**. The outcome of patients with ALL in Romania improved continuously over the last decade, despite multiple logistic problems such as the lack of specific diagnostic tools as for example genetic analysis or minimal residual disease monitoring (MRD). Nevertheless, correct anti-leukemic treatment can be properly delivered, as well as efficient supportive therapy and there are promising signs that MRD analysis can also be introduced nationwide. Romania needs to adhere to international optimization studies as soon as possible.

ENDOCRINE COMPLICATIONS IN PATIENTS WITH HEMATOLOGIC DISORDERS.

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The survival of patients with hematologic disorders has improved nowadays as a result of enhanced medical care that leads to diagnosis in the early stages of the disease and the new medication used to treat these patients. Therefore, the prevalence of long-term complications (endocrine, pulmonary, cerebrovascular, neurologic, second neoplasia) has increased. The endocrine disorders are among the most frequent long-term adverse effects that appear in patients with hematologic diseases. The survivors often experience ovarian insufficiency, oligo-azoospermia, impaired linear growth and pubertal development, thyroid disorders, insulin resistance, metabolic syndrome, osteopenia/osteoporosis. The endocrine system is affected both by chemotherapy and radiotherapy and also long-term endocrine complications can follow bone marrow transplantation due to the graft versus host disease. Early diagnosis of endocrine dysfunction in these patients and the early replacement therapy may improve the quality of life and decrease the risk of premature death.

MINIMAL RESIDUAL DISEASE EVALUATION IN ACUTE LYMPHOBLASTIC LEUKEMIA– ACTUAL DATA.

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Minimal residual disease (minimal residual disease, MRD) defined by the presence of morphologically detectable leukemic cells, can be detected by immunophenotyping and advanced techniques of molecular biology. In children with ALL, the level and evolution of MRD are independent prognostic factors; MRD negative patients are associated with the best prognosis. The clinical benefits of MRD monitoring include tracking response to chemotherapy, relapse early detection and choice of the appropriate therapy according on individual risk class based on different levels of MRD at various points of time during therapy. Analysis of MRD provides information on disease progression, response and efficacy as well as important data on leukemia cell biology. Currently three techniques can be used to determine the minimal residual disease:
1) Immunophenotyping by flow cytometry to detect phenotype "associated leukemia";
2) PCR techniques to detect chromosomal aberrations;
3) PCR techniques to detect specific regions of gene rearrangements of Ig and TCR [1].

In the course of induction therapy, the detection of MDR reflects the response to cytotoxic therapy: the absence or low levels of MRD in the bone marrow are associated with a favorable prognosis. The absence of the end of induction of MDR is associated with a reduced relapse rate of 2-10%, and a high level of MDR at the end of induction is associated with a relapse rate of 70-100%. Statistical analyzes showed that MDR status at the end of induction is the most important prognostic factor independent of other factors such as age, WBC count, immunophenotype, karyotype, response to prednisone. At the end of induction characteristics cytogenetic and morphologic response MDR reclassify patients into four risk groups: low, standard, high and very high. AEIOP-BFM 2000 study recommends MDR monitoring on days 33 and 78 for the stratification and selection of treatment intensity post-consolidation.

FLOW CYTOMETRY METHODOLOGY AND ITS CONTRIBUTIONS TO MRD DETECTION.

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Minimal residual disease (MRD) refers to the small number of malignant cells that remain after therapy when the patient is in remission and shows no symptoms or overt signs of disease. MRD diagnostics has proven to be the strongest prognostic factor, allowing for risk group assignment into different treatment arms, ranging from significant treatment reduction to mild or strong intensification. The morphological examination of peripheral blood or bone marrow smears, although still an indispensable part of routine laboratory testing, is clearly insufficient for patient management, and clinicians should not ask themselves whether to look for MRD or not, but how and when. Multicolour flow cytometry (MCFC) constitute an important used techniques for MRD detection.This oral presentation shows immunophenotyping issues (pre-analytical and analytical) for the detection of minimal residual disease in acute lymphoblastic leukemia and also our results interpretation.

CLINICAL HAEMATOLOGY SECTION
POSTERS SESSION

PLASMACYTOMAS AT A PATIENT WITH REFRACTAR MULTIPLE MYELOMA- CASE REPORT.

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Introduction: Multiple myeloma is a malignant hematological disease characterized by plasma cells proliferation in the bone marrow, which produces a disturbance of the normal function of the bone marrow, bone destruction, secretion of monoclonal protein in the blood and/or urine and immune injury. Plasmacytomas are malignant plasma cells tumors that develop in soft tissues (extramedullary) or skeletal bones. Myeloma tumors are rare identified to the onset of the disease but may occur in the evolution of multiple myeloma.
Case presentation: A woman, 56 years old, is admitted in our clinic in the February 2015 showing left frontal tumor formation and accusing pain lumbar-sacral spine and lower limbs. CT examination detected left frontal formation by 80 mm, left fronto-temporal formation by 24 mm and multiple osteolytic lesions at the skull, ribs and spine. **Lab analyzes was performed and we** found 20% marrow plasma cell infiltrate, ESR-140mm/ h, total proteins-10,92mg/dL with M gradient of 3,21g/dl and IgA- 22,47g/l, which confirm the diagnosis of IgA secretory multiple myeloma. She was given 8 cycles of chemotherapy consisted in Velcade +Epirubicin+ Dexamethasone and we got favorable response on the marrow infiltrate, normal values of the total proteins and IgA but no effect on the plasmacytomas size. Subsequently the patient was performed 10 sessions of 30 Gy radiotherapy, with minimal tumors regression. In the February 2016 the patient suffered a right femur fracture, reduced by metal rod in the May 2016 and after 2 months in the same place developed a 10 cm plasmacytoma. In that moment we decided to resume chemotherapy with Vincristine + Caelyx + Dexamethasone, but she had unfavorable response and died in the July 2016.
Conclusions: Plasmacytomas are generally radio-sensitive tumors, but in our case we haven't reached the expected effect. Chemotherapy has had a positive effect on marrow plasma cell infiltrate and on monoclonal gradient value, but without effect on the size of plasmacytomas.
Keywords: plasma cell, myeloma, therapy.

KARYOTYPE ANALYSIS IN A GROUP OF 161 PATIENTS WITH MDS.

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In 2012 it is published the IPSS-R, which includes several chromosomal abnormalities that are layered into 5 groups risk cytogenetics, compared with 3 in IPSS, emphasizing the importance karyotype as a prognostic factor in MDS.
We present evaluation of 76 patients (out of 161 patients enrolled), which were performed cytogenetic examination. Chromosomal abnormalities were divided into risk groups, according to the IPSS classification. We analyzed 161 patients diagnosed with de novo MDS in Hematology Departments of Fundeni, Colentina and Coltea, during 1995 to 2015, who were followed for a period of 36 months, excluding the cases unclassifiable. Evaluation of patients included cytogenetic tests: karyotype of bone marrow by indirect method: cell cultures 24 and 48 hours; slides were stained by G banding technique (resolution bands: 450-550 bands). 20 metaphases were evaluated in laboratory of Fundeni and "Victor Babes" Institutes in Bucharest and the Genetic Center - Cluj Napoca.
It was performed statistical analysis, using Microsoft Office Excel 2007 for Windows, SPSS (Statistical Program for Social Sciences) version 21.0 for Windows, EpiInfo 3.5.1.
It was revealed normal karyotype in most patients, but also hiperdiploidy, del 12p, trisomy 8, del 5q, monosomy 2, monosomy 16, izocromozom 17q, complex karyotype with 3 anomalies, including del (5) (q32;qter), abnormalities of chromosome 7 and other anomalies: 52,XXX, +4,+6,+8,+17,+21.
46,XX,t(2;6)(p16;q22.1),t(5,11)(p14;q23.1), del(13)(q10;14.1).
46,XX,del(11)(p14;pter),t(3,6)(q12;q26), 45,XY,rob(13;15)(q10;q10).
In the subgroup analysis according karyotype distribution observed: mainly karyotype with good prognosis (good): 61.3%. It observed statistically significant association between karyotype and

neutrophil count (p = 0.03), infectious complications (p = 0.004), platelet count (p = 0.003), bleeding complications (p = 0.01), cytopenias (p = 0.1), dysplasia (p = 0.01), the percentage of peripheral blasts (p = 0.0008), and medullary blasts (p = 0.00), LDH (p = 0.03), the rate of conversion in AL (p = 0.00) and death (p = 0.01) and the median duration of overall survival (p = 0.003). No statistically significant association was observed between ferritin and karyotype (p = 0.6) or response to treatment (p = 0.17).
Conclusions: There are scoring systems that include hematologic, cytogenetic and clinical features as being reproductible and validated as prognostic models. It remains to be seen how cytogenetics influence the response to treatment in the era of new therapeutic agents.

RESEARCH OF SECOND HAEMATOLOGIC MALIGNANCY ÎN SUBJECTS DIAGNOSED WITH HAIRY CELL LEUKEMIA.

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Hypothesis:
The development of a second haematologic malignancy may be the expression of the existence of two clones competing for domination. Elimination of the dominant clone gives way to the expression of the second clone, resulting in the development of the second haematologic malignancy.

Material and methodology:
Two subjects diagnosed with hairy cell leukemia developed over time the second haematologic malignancy: marginal zone B cell lymphoma.
The analyzed parameters were:
- the age of the diagnosed patients;
- the severity of bone marrow involvement;
- therapy;
- minimal residual disease;
- timeframe between the remission of hairy cell leukemia and the development of the marginal zone B cell lymphoma;
- evolution of the second haematologic malignancy;
- phenotypic pattern of the second haematologic malignancy;histopathological re-evaluation of the bone marrow assay and of the spleen.

Results:
- Female patient (NI): 45 years old at diagnosis (2010);
- Male patient (PT): 60 years old at diagnosis (2013);
- Severity of bone marrow involvement: NI 90%; PT 65%;
- Therapy:
  - Interferon and splenectomy for female subject NI;
  - Cladribine (Lytak) and interferon for male subject PT;
- Evaluation of the minimal residual disease:
  - Female subject NI: 2.6% (B lymphocytes: CD 19 +, CD103 +, CD 25 +, CD 11c+), 18 months since the start of the treatment, and 0.5% 52 months since the start of the treatment;
  - Male subject PT 0.8% (B Lymphocytes: CD 45 ++, CD 19 +, CD 20 +, CD 103 +, CD 11c+), 6 months since the start of the treatment, and 0.2% 28 months since the start of the treatment;
- Timeframe between the remission of the hairy cell leukemia and the development of the marginal zone lymphoma was 30 months in female subject NI and 28 months in male subject PT;
- Evolution of the second haematologic malignancy: indolent;
- Immunophenotipic expression of the second clone: B lymphocytes CD 19+, CD 25-, CD103-, CD11C +/-, CD 20++, CD5- in female subject NI and CD5+/- in male subject PT, CD 43-, CD 79B++
- Histopathological re-evaluation of the histological material taken during the 2010 splenectomy indicates associated to hairy cell leukemia involvement a minimal lesion suggesting splenic marginal zone lymphoma.

Conclusions:
- different therapies the two subjects;
- the timeframe between the starting of the therapy and the development of the second haematologic malignancy was only 28, respectively 30 months;
- detection of minimal lesions suggesting splenic marginal zone lymphoma even at the moment of hairy cell leukemia diagnosis in female subject NI;

→ all these are arguments in favour of the existence of two malignant clones, with the clinical expression of the second clone after the therapeutical elimination of the first clone.

INTERCELL EXCHANGE OF THE GENETIC MATERIAL – POSSIBLE MACHANISM OF TUMORAL PROGRESSION.

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Hypothesis:
The progression of haemathologic malignancy cannot be 'mathematically' explained through cell proliferation and apoptosis. Contamination of the normal cells through transfer of genetical material from the malignant clones' cells represents a possible mechanism of tumoral progression.
Materials and methodology:
The patterns of the BCL 2 în the biopsies taken from subjects with T or B NHML diagnosis were analyzed.
Conclusions:
Contamination of normal cells through transfer of genetic material from malignant clones' cells represents a potential mechanism of progression for haematologic malignancies.

THROMBOTIC COMPLICATIONS IN CHRONIC MYELOPROLIFERATIVE DISORDERS.

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Background. Thrombotic complications are major cause of morbidity and mortality in patients with myeloproliferative disorders. The incidence of thrombotic events in myeloproliferative disorders does not correlate significantly with gender or platelet counts, but rather with age and a history of cardiovascular disease and/or thromboembolic events. Low-dose aspirin significantly reduce the risk of thrombotic complications in polycythemia vera (PV) patients, and is used in essential thrombocythaemia (ET). Hydroxyureea, interferon-α and anagrelide and are currently used treatments.
Aim. We performed a retrospective study on a group of patients with myeloproliferative disorders, especially TE, classified according to WHO 2008 guidelines on treatment response and complications occurring in these patients.
Methods. We retrospectively studied 107 patients, 45 male and 62 female with a median age of 54 years (30-82). Thrombosis at diagnosis were present in 35/107 patients. Median platelet count was 830 x 109 / L (650-2300 x 109 / L), splenomegaly was present in 41 patients, and fibrosis in 48 patients. Patients were treated with Hydroxyureea (HU) (34 patients), 53 patients received anagrelide, 20 patients received interferon-α.
Results. Hemoglobin level and platelet count was similar in the 2 groups of patients (group of patients who received only HU and the group of patients who received anagrelide, interferon). The number of leukocytes in the blood/white blood cells count (WBC) and platelet count was correlated with thrombosis at the time of diagnosis. In the study group it was found following risk factors: Hypertension 30.4%, smoking 17.5%, diabetes mellitus 4.3%. Also, the investigation of thrombotic markers revealed: JAK2 mutation 31%, elevated homocystein level 7%, Factor VIII elevation 10%, Protein S deficiency 9%, Factor V Leiden mutation 5%, Fibrinogen 21%, antiphospholipid antibody syndrome 6.1%, Lupus anticoagulans 3,2%, Factor IX elevation 1,7%, AT III deficiency 1,4%, Protein C deficiency 0,6%, prothrombin mutation 0,5%. Thrombotic events consisted of 18 arterial thrombosis (7 coronary disease, 7 stroke, 4 intestinal infarct) and 16 venous thromboses (10 deep and 4 splanchnic vein thrombosis, 2 cerebral sinus thrombosis).
Conclusion. There is an increased incidence of thrombotic events in myeloproliferative diseases. They are influenced by the presence of thrombogenic risk factors and thrombotic markers.

HIPERFERITINEMIA IN MYELODISPLASTIC SYNDROME,CORELATION WITH EVOLUTION AND SURVIVAL OF PATIENTS.

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Background. The myelodysplastic (MDS) patients have anemia and many require red blood cells (RBC) transfusions leading to iron overload. Hematological improvement during iron chelation therapy was revealed more than twenty years ago and seems to be more frequent after introduction of Deferasirox. The most simple test assessing iron overload is serum ferritin concentration.
Aims. Assessment of hyperferritinemia incidence in MDS patients at the moment of MDS diagnosis, and correlation between ferritin level and evolution an survival in patients diagnosed with MDS.
Methods. The retrospective data collection from a single center experience (Department of Hematology County Hospital, Timisoara) between January 2005 and July 2015 included 150 patients (86 men and 64 women) with MDS.The patients had complete blood count and serum ferritin level, and complete follow-up data.
Results. Ferritin level above 1000 ng/mL was found in 61 patients (40.66%) (Group 1) and ferritin level ≤1000 ng/mL in 89 patients (59.34%) (Group 2). Most patients with significant hiperferritinemia, were RBC transfusion dependent (76% of patients). Among

patients with ferritin level ≤1000 ng/mL, 38% were RBC transfusion dependent. Serum hemoglobin concentration was lower in Group 1 patients in comparison with Group 2 patients (6.8 g/dL vs 9,3 g/dL, p< 0,004). The most frequent MDS subtype in Group 1, were patients with refractory anemia (RA) (33%), compared with patients with ferritin ≤1000 ng/mL - 16% (p<0,05). According to IPSS score, there were no differences between studied groups. Median follow up was 14 months. There was an improved overall survival (OS) in RBC transfusion independent patients compared to RBC transfusion dependent patients, mean OS was not significantly statistically different in studied groups. No correlation was found between ferritin level and time to acute myeloid leukemia(AML) transformation.

Conclusions. Hiperferritinemia >1000 ng/mL does not influence survival and time to AML transformation in MDS patients. The most frequent MDS subtype in patients with ferritin level >1000 ng/mL was MDS RA. Among patients with ferritin level >1000 ng/mL 76% were RBC dependent.

THE RESULTS OF TREATMENT WITH IMATINIB MESYLATE IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA. SINGLE CENTRE EXPERIENCE.

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Background. Imatinib Mesylate, a Tyrosine Kinase inhibitor, is one for chronic myeloid leukemia (CML) in chronic phase (CP). During therapy, a few patients develop myelosuppression. Adverse side-effects of the drug could be: edema, nausea, vomiting, diarrhea, cramps and cutaneous reactions. Adverse hematologic side-effects could include anemia, neutropenia, and thrombocytopenia.**Aims**. The aim of this study was to evaluate the results of treatment and the safety of imatinib as first line therapy in patients with newly diagnosed CML-CP.

Methods. Between January 2008 and July 2015, 101 patients with Ph+CML-CP were included in the study. They were diagnosed in Department of Hematology, County Hospital Timisoara. Eligibility criteria included age 18 years and older, ECOG performance status of 0 to 2, adequate hepatic and renal functions, no prior imatinib therapy, non-pregnant patients. CML-CP was defined as less than 10% blasts and less than 10% basophils in the peripheral blood and bone marrow and a platelet count between 100x109 L and < 1000x109 L. Therapy was initiated with imatinib 400 mg orally daily and patients were monitored for any adverse effects.

Results. Out of 101 cases with CML-CP included in the study, male: female ratio was 0.9:1.3 with median age 47 (ranged from 18-75). After starting Imatinib a CHR was achieved at 3 month by 88.3% patients.The CyR achieved was major in 78%(with 60% CCR). The molecular response was complete in 31% and major in 36% patients.The doses were increased in 26 patients and improved response was achievd in 16 patients. Six patients were switched to Dasatinib and eight to Nilotinib.The median follow-up was 60 month(range 20-82) and under Imatinib was 52 months.The 14 patients died,8 of blastic transformation.The study showed that the commonest hematological side effects were grade 2 anemia (15%), followed by leucopenia 13%, and thrombocytopenia 9%. The most common non-hematological adverse effects were superficial edema and weight gain 32%, followed by musculoskeletal pain 31%, then gastro-intestinal (vomiting, diarrhea) 11%.

Conclusions. Data indicated that imatinib mesylate remains effective for the most of the patients is a well tolerated drug, and all adverse effects could be managed for patients with CML-CP. The most common hematological side effect was anemia, while the non-hematological side effect was fluid retention.

THE RESULTS OF THERAPY IN ELDERLY PATIENTS WITH ACUTE LYMFOBLASTIC LEUKEMIA. RETROSPECTIVE STUDY.

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Background. Acute Lymphoblastic Leukemia is uncommon and less curable in patients over 60 years of age because of a greater resistance to chemotherapy, a relative inability of elderly patients to face the toxic effects,the complications of therapy and influence of co-morbidities.

Aims. We presented our experience of 59 consecutive cases of ALL of elderly age and evaluation of treatment respons.

Methods. The patients were hospitalized in the last ten years,median age was 67 years (range 61-85 yeaers). L2/L1 FAB classification: 49/10; Median WBC was 18xl09L (range 2-189); Male/Female ratio was: 25/34. Forty-six (77.96%) belonged to B cell lineage (pre-pre-B 11, common 30, pre B-5) and 13 (22.04%) to T cell lineage (pre-T staged). Philadelphia chromosome was present in l4 patients (23.72%).

Out of the 59 revisited patients, 38 patients (median age 66 years, range 61-75, good performance status and without co-morbidity factors), received an intensive treatment such as ALL protocols. In the remaining 21 older patients (median age 77 years) and those with severe coexisting cardiac, pulmonary, renal and hepatic disease, a gentle chemotherapy including prednisone and vincristine, 6-mercaptopurine and methotrexat was utilised.

Results. 12 patients (31.57 %) of the group treated with curative intent died during the induction phase; 27 patients (71.05%) achieved complet remission (CR) and, at present, 6 patients are alive at 10, 15, 18, 21, 24 and 26 months Out of 21 patients receiving less intensive and supportive treatment only 4 achieved a short CR: other patients had an early relapse and dead.

Conclusion. Our data demonstrated that immuno-phenotypic patterns of patients is very important for survival and prognosis. The younger patients who can well tolerate an aggressive tratment could benefit of this approach, because of it is possible to achieve longer survivals.

DEBUT WITH BUDD-CHIARI SYNDROME AND POLYCYTHEMIA VERA IN A PATIENT DIAGNOSED WITH HEREDITARY THROMBOPHILIA.

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Introduction: Hereditary thrombophilia is characterized by a clotting abnormality which increases the risk of thrombosis, most commonly involved are factor V Leiden and prothrombin G20210A. The preferred treatment is anticoagulation medication in patients without risk of bleeding.
Budd-Chiari syndrome is a condition caused by hepatic vein occlusion. The syndrome may be acute, chronic, fulminant or asymptomatic. Treatment consists of anticoagulation treatment, symptomatic or surgical treatment.

Polycythemia Vera is a neoplastic disorder characterized by excessive growth of erythrocytes, leukocytes and platelets. Treatment consists of cytoreduction and phlebotomy sometimes associated with low-dose aspirin.

Case presentation: We present the case of a patient D.N., aged 34 years diagnosed in February 2010 with the Chronic Myeloproliferative Syndrome type Polycythemia Vera JAK2 positive based on clinical examination (splenomegaly), blood counts and bone marrow biopsy and the subsequent treatment with Interferon, with favorable development. Also in February 2010 she was diagnosed with Budd-Chiari syndrome - portal vein thrombosis following biochemistry tests, coagulation tests, abdominal ultrasound and abdominal computer tomography and subsequently treated with oral anticoagulation. In May 2014 treatment was adjusted with Clexane in regards to the patient's desire to procreate, genetic tests conducted have highlighted the MTHFR mutation (A1298) heterozygous genotype, heterozygous gene PA11 positive 4G/5G heterozygous mutant Factor V Leiden positive, specific for hereditary thrombophilia. The pregnancy was carried out without complications, with postpartum adjustment and maintaining normal blood count and coagulation tests. The patient is still with the same regiment as she still nursing.

Results - Conclusions: The patient presented with a hematologic malignancy and obstructive venous syndrome for which treatment was initiated with interferon and oral anticoagulants, treatment adjustment in regards to the patient's desire to procreate. The genetic tests performed revealed a hereditary coagulopathy.

DIFFUSE LARGE B-CELL LYPHOMA AS SECONDARY HAEMATOLOGICAL MALIGNANCY AFTER CHRONIC LYPHOCYTIC LEUKEMIA – CASE REPORT.

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The chronic lyphocytic leukemia (CLL) it is one of the most ferquent hematologic disease among the elderly, caractherized by monoclonal B cell lyphocytosis (> 5000 µl, examined with flow cytometry). The major symptoms of the disease are: asthenia, fatigue, nocturnal sweating, hepato- and/or splenomegaly, repeated infections, lymphadenopathy. The prognostic of CLL is determined by genetic markers, age and patient comorbidities, the survival can be between a few years and more than 20 years. The patients with CLL has a 5-7 times higher risk to develop a secondary malignancy. Our study presents the case of a 66-year-old female patient with CLL stage I/A diagnosed in Hematology and Bone Marow Transplant Section Targu Mures in september of 2011 followed by periodic hematological controls without the need of any

specific therapy. In september of 2015 the patient enters the Otorhynolaryngology Clinic of Sfantu Gheorghe with the following plaints: tonsillar hypertrophy, dysphagia and local compressive symptoms. The tumor biopsy followed by histpathological and immunohistochemical examinations confirms the diagnosis of a diffuse large B-cell lyphoma, the patient being in good general conditions, without palpable lyphadenopathy, presenting a slight hepato-splenomegaly. Starting from december 2015 the patient receive monthly chemo- and immunotherapy (3 CHOP and 5 RCHOP). At this stage, the disease presints o positive prognostic.

CHRONIC LYMPHOCYTIC LEUKEMIA AND ASSOCIATED MALIGNANCIES.

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Introduction. Chronic Lymphocytic Leukemia is a chronic lymphoproliferation characterized by malignant proliferation and accumulation of a clone of small lymphochytes (bone marrow and blood, secondary in spleen, lymph nodes and other organs) apparently mature but immunologically incompetent. It is the most common form of leukemia in adults (30% of leukemia, with a 20/100.000 individuals/year incidence, maximum frequency between the ages of 50 and 70, exceptional under the age of 40. The disease is characterized by deficient cellular immunity (both by disease and treatment), increased risk of developing infections, autoimmune phenomena and increased incidence of secondary malignancy.
Purpose. The purpose of this study is to evaluate the rate of secondary malignancies development, depending on the type of cancer, in patients with chronic lymphocytic leukemia.
Material and method. A retrospective study was conducted in patients diagnosed with chronic lymphocytic leukemia regardless of the disease stage (Rai/Binet classification), age, sex or undergoing treatment, in evidence of Timisoara Hematology Clinic, period January 2006-December 2015. Diagnosis was established on cell blood count, bone marrow aspirate plus/minus immunophenotyping test. Types of secondary cancers seen in patients were divided into solid tumors, non-melanoma skin cancer and hematologic malignancies. The cancers that preceded the diagnosis of Chronic Lymphocytic Leukemia were also recorded.
Results. 500 patients were included in the study. Mean age was 61,75 years. In terms of stage disease, 25% patients were stage A, 35%, stage B and 40% stage C. A total of 77 patients with secondary malignancies were indentified. Lung cancer was present in 20% of patients, non-melanoma skin cancer and colo-rectal cancer, each in 18%, Richter's syndrome and prostate cancer in percentage of 10% per, neoplasm of the bladder and breast neoplasm were present each in a proportion of 8%, 6% of patients had cancer of the cervix and 2% had other types of cancer.
Conclusions. Chronic Lymphocytic Leukemia patients show a higher risk of neoplasia development. Genetic susceptibility, depressed cellular immunity, undergoing treatment and old age
represent risk factors of malignancy appearance. Chronic Lymphocytic Leukemia patients need long-term periodic monitoring in order to identify any clinical or laboratory changes.

INFLUENCE OF SYSTEMIC MANIFESTATIONS ON PATIENTS EVOLUTION WITH MULTIPLE MYELOMA.

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Background. Multiple myeloma (MM) is a malignant plasma cell proliferation with an annual incidence growing about 4.5 / 100,000 population , a condition that often results in patients middle-aged and elderly . The disease is characterized by the presence of a plasma cell infiltrate higher than 10%, the existance of monoclonal protein in blood and/or urine and lytic bone lesions.
Aims. The study aims was to evaluate systemic manifestations and the incidence of their influence on patients evolution diagnosed with MM.

Methods. In the retrospective analytical study were included 85 patients diagnosed with Multiple myeloma at the Hematology Department of Emergency Country Hospital from Timisoara during the period January 2011 and January 2016. Diagnosis was established based on a complete clinical examination, complete blood count, biochemistry tests, secretion of monoclonal proteins,

bone marrow aspirate/biopsy, radio-imagistic investigations (Rx, CT, MRI).
Results. The average age of the patients included in the study was 61 years and the distribution by sexes indicated that 56% were males and 44% females. By studying the concentration of monoclonal immunoglobulin (Ig) we found that 51% of the patients present IgG, 36% IgA, 2% IgD, 1% IgM and 10% monoclonal free light chains. Hyperviscosity symptoms were found on 9% of the patients especially on those presenting IgA and were the most frequent manifestations. 41% of the patients presented kidney failure at diagnosis and in 59% of the cases it was secondary developed. The bone infiltrate leads to pain which is the most frequent symptom and the abnormal bone metabolism determines hypercalcemia in 25% of the patients at the initial diagnosis. The neurological manifestations were found both at diagnosis (25%) but mostly on the evolution of the disease (75%). Normochromic normocytic anemia was found on 73% of the patients at the moment of diagnosis and later on at almost all of the patients. Gastrointestinal disorders and cytopenias such as neutropenia and thrombocytopenia developed secondary to chemotherapy and the infections caused by the alteration of cellular immunity and humoral response depended on the type of chemotherapy administrated.
Conclusions. The evolution of the patients and default rate of survival are correlated with the presence of the systemic manifestations. Even if there was made an important progress, MM still has an unfavorable prognosis. Death occurs secondary to renal failure, infections or hemoragy caused by pancytopenia associated to a high plasma cell infiltrate.

EXTRANODAL DETERMINATIONS IN HODGKIN LYMPHOMA AND THEIR IMPACT ON THE RESPONSE TO CHEMOTHERAPY .

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Introduction. Hodgkin lymphoma is charaterized by the presence of Sternberg-Reed cells or their variants surrounded by benign reactive cells: lymphocytes, neutrophiles, plasmocytes and fibroblasts.
Purpose. The study proposes the evaluation of the response to chemotherapy of the patients with extranodal determinations.
Methods. We conducted a retrospective analytical study on 100 patients between January 2009 and December 2014, diagnosed with Hodgkin lymphoma at the Hematology Department of Timisoara. The main method used for the identification of the extranodal determinations was the CT followed by bone marrow aspirate.
Results. Of the total 100 patients, 57% are male sex and 43% females with ages ranging between 20 and 80 years. 51% of the patients showed extranodal determinations. The most frequent were the medullary ones (33,33%), being followed by the pulmonary ones (19,6%) and the mediastinal ones (19,6%). As for the response to the first line of treatment (polychemotherapy according to ABVD protocol) at the patients with extranodal determinations, the rate of complete response is significantly higher at patients with mediastinal tumor (60%), followed by the rate of complete response of those with secondary medullary determinations (23,52%) and by those with secondary pulmonary determinations (20%).
Conclusion.The extranodal determinations proved to be frequent in Hodgkin Disease, the medullary impairment being predominant. Referring to the response to the treatment, it proved to be better for patients showing secondary mediastinal determinations.

OPTIMAL THERAPEUTIC RESPONSE IN HODGKIN LYMPHOMA.

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Introduction. Hodgkin lymphoma is a rare malign disease with an incidence of 2 to 4 cases by 100,000 per year. It is characterized by the presence of the Sternberg Reed cells and is a malign proliferation of the lymphoid tissue.
Purpose. The study proposes the evaluation of the response to the treatment applied to the patients diagnosed with Hodgkin Disease.
Methods. We made a retrospective analytical study on 80 patients diagnosed with Hodgkin Lymphoma at the Hematology Department of Timisoara during the period January 2010 and December 2015. The diagnosis and the staging were established based on the clinical and paraclinical investigations (complete blood count,

medullary aspiration, biochemical tests, lymph node biopsy with histopatological and immunohistochemical investigations , radio-imagistic investigations). The first line treatment was applied in accordance with ABVD respectively BEACOPP protocol.

Results. The patients were included within 3 groups of age: between 20-40 years, 40-60 years and 60-80 years with the male sex prevalinig (72,5%).

Of the 80 patients, 49 (61,25%) underwent polychemotherapy according to ABVD protocol while 31 (38,75%) patients were administrated polychemotherapy according to BEACOPP protocol. The rate of complete response is higher for the patients treated according to ABVD (42,86%) protocol compared to those who were treated with polychemotherapy in accordance with BEACOPP (33,33%) protocol. As for the disease progress, it proved to be more frequent for the patients treated with polychemtherapy of ABVD protocol (20,4%).

Conclusions. Despite the progress made in the field of Hodgkin disease treatment, the ABVD protocol proves to be further on the most efficient first line therapy for this disease with a complete response rate significantly higher than other therapeutic schemes.

THE MANAGEMENT OF A REFRACTORY CASE OF HODGKIN LYMPHOMA IN THE ERA OF ANTI-CD30 ANTIBODY DRUG CONJUGATES.

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Introduction: LH represents a neoplasia of the lymphoid tissue, characterized by the presence of the Reed-Sternberg malignant cells, surrounded by a reactive population formed by T and B lymphocytes, neutrophils, eosinophils, histiocytes and plasmacytes. The etiology is still incompletely elucidated. The start of the illness is insidious and consists in the occurrence of predominantly supradiaphragmatic adenopathies, weight loss, fever and profuse sweating. The evolution and the prognosis of the disease varies depending on the stage it is detected.

Case report: We present the case of a male patient, aged 58 years, from the urban area, without significant pathological personal history, diagnosed in 2008 with LH. At diagnosis, the patient presents asthenia, moderate fatigability. Objective, is discovered right latero cervical bilateral adenopathy with the maximum diameter of approximately 6-7 cm in the right side, mobile, painless, right supraclavicular, right retroauricular and bilateral auxiliary of approximately 1-2 cm, accompanied by night sweats and weight loss. After clinical-biological investigations were conducted, in order to exclude an inflammatory process, osteo marrow biopsy is done and immunohistochemical examination that orients the diagnosis to an LH form with nodular clerosis, stage II Bx on the CT basis 4 regions and on the presence of the symptomatology of type B. Chemotherapy treatment ABVD type has been initiated with attainment of a partial remission after 6 applications, evidenced by PET/CET. Simultaneously the patient is diagnosed with type II Diabetes, treated with ADO, with a favorable evolution. Later, in 2010, the patient returns with a influenced general state, asthenia and marked fatigability, subfebrilities, hyperglycemia, suspecting a relapse of the disease. Performs BOM and MRI which confirms the under diaphragmatic relapse and detects secondary bone determinations and the patients is III Bx restaging. Chemotherapy treatment is established according to the BEACOPP protocol and performs 6 applications after that is revaluated though PET/CT which highlight an active metabolic splenic lump and retroperitoneal and internal mammary adenopathies, which is why in 2012, chemotherapy is resumed obtaining a partial remission in 0.3.2013 highlighted through PET / CT scan performed after 6 cycles. The patient is periodically hematologic reassessed until 09.2015 when he returns with a profound influenced general state, accusing dry cough, dyspnea, colicky abdominal pain, profuse sweating accompanied by the presence of some left axillary adenopathies of approximately 2 cm, mobile, painless. The patient`s condition worsens during hospitalization, and after multiple clinical, biological and imagistic (Rx thorax, CT thorax, CT 4 regions) investigations, multiple cardiac affections are highlighted for which specific treatment is recommended. Biopsy by needle puncture is performed (from left axillary lymph node) with histopathology and imunohistichimic exam, which pleads for an LH classic form with mixed cellularity (CD 30 positive). The PET/CT exam highlights left internal mammary adenopathy relapse with invasive character, left axillary adenopathies, persistent splenic tumor and right pectoral muscle metabolic active node. In 03.2016, Brentuximab Vedotin (1.8 mg / kg) treatment is established according to the protocol with a favorable evolution and improvement of symptoms. During the Brentuximab Vedotin treatment, the persistence of a easy form of normochromic normocyte secondary anemia, without other significant changes of the hematologic and biochemical picture. The glycemia values are in the normal limits, the patient is still being

under treatment with ADO and specific treatment for cardiological diseases.
Conclusions: Both evolution and prognosis are marked by the refractory character by converting in to second histological type. However, the relapse after two lines of treatment and the CD 30 positivity include the patient in the treatment programme with Brentuximab Vedotin, registering until present a favorable evolution to the above mentioned treatment.

HYPERCALCEMIA IN MULTIPLE MYELOMA. IMPACT ON DISEASE EVOLUTION AND PROGNOSIS.

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Introduction. The multiple myeloma represents a malign plasmocyte proliferation. The tumor, its products and the response of the host body determine the occurrence of malfunctions of the organs, aches or bony fractures, renal impairment, susceptibility at infections, anemia, hypercalcemia, occasionally coagulation abnormalities, neurologic symptoms and hyperviscosity signs.
Purpose. The study proposes the evaluation of the hypercalcemia impact on the evolution and prognosis of the patients diagnosed with multiple myeloma.
Methods. We conducted a retrospective analytical study on 77 patients diagnosed with multiple myeloma at different stages of disease evolution and under the supervision of the Hematology Department of Timisoara since January 2010 and until December 2015. The diagnosis of multiple myeloma was established based on the presence of monoclonal immunoglobulin in either the serum or the urine, on the excretion of urine light chains (kappa or lambda), the presence of the medular plasmocyte infiltrate of more than 10% , reveal of bone lessions. The patients have been checked up both clinically and paraclinically (complete blood count, biochemical tests, radio-imagistic investigations).
Results. The average age of the patients was 60 years and the distribution by sexes indicated it was prevailing for females. Of the total 77 patients, 24 (31,2%) patients were subject to polychemotherapy according to the VAD protocol, 42 (54,5%) Velcade in association with Dexamethasone and 11 (14,3%) Velcade therapy in association with Dexamethasone and Caelyx. From statistical point of view, there was revealed a significant difference (p=0.024) regarding the persistance of hypercalcemia at patients who were subject to VAD compared to those who were administrated Velcade in association with Dexamethasone and Caelyx, in the sense that hypercalcemia was more frequent for the latter. The same significant difference, from statistic point of view (p=0.046) was noticed between the group who was administrated the treatment with Velcade and Dexamethasone and the group where the Velcade was associated with Dexamethasone and Caelyx. Further to the review of the global response to the treatment, it was noticed that patients where the hypercalcemia is persistent show higher relapse rate.
Conclusion. Hypercalcemia proved to be one of the most frequent complications caused by the multiple myeloma as it can be present both at the diagnosis and further in evolution. Comparing the VAD therapy with the Velcade associated with Dexamethasone and respectively, Velcade associated with Dexamethasone and Caelyx at patients with hypercalcemia, it was revealed that the response rate to chemotherapy is better for the patients treated with Velcade in association with Dexamethasone.

TREATMENT OF NON – HODGKIN LYMPHOMA IN A PATIENT WITH CHRONIC VIRAL HEPATOPATHY . CASE PRESENTATION.

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Introduction. Non Hodgkin Lymphoma represents a neoplasia of the immune system, a diverse group of defects that originate in the lymphatic system with cellular proliferation in the lymphoid organs or in other tissues that contain lymphoid structure. The ethiology of the pathology involves genetic factors, infections, environmental factors, immunodeficiency, inflammations and exposure to toxic substances.
It expresses through a wide variety of clinical, histological, genetic and molecular manifestations.
Case report. We present a case of a 40 year old patient who was diagnosed in September 2015 with marginal zone lymphoma. The patient performed a routine blood test that revealed leucocytosis (40.210mm3) with lymphocytosis (31.210mm3). The clinical exam identifies a slight splenomegaly, fatigue and loss of appetite. Further specific investigations were performed

as a CT scan of the 4 regions, which showed hepatosplenomegaly, multiple lymphadenopathies on the examined regions and the bone marrow aspirate that expressed a 51% lymphoid infiltration on the examined probes. Peripheral blood immunophenotype and histopathological examination of the bone marrow confirms the diagnosis of Non Hodgkin malign lymphoma with marginal zone B cells staged IV A. After further investigations, the patient was diagnosed with HBs Ag positive, being directed toward the Clinic of Infectious diseases for HBV.
In accordance with the protocol, the chemotherapy consisting of CHOP II applications (02.2016) was initiated with a favourable outcome, but the third application (03.2016) has been delayed due to a hepatocytolisis syndrome (ALAT=161U/I; ASAT=65 U/L). We mention the fact that the patient follows an antiviral therapy with Entecavir from 01.2016 till present. After the recovery of the liver function tests, it was decided to initiate an alternative chemotherapy with CVP IV applications (04.2016-06.2016) associated with II applications of Mabthera with favourable outcome.
Conclusion: In the B cell non Hodgkin lymphoma malignancies, associated with active hepatitis, the prophylactic antiviral treatment should start prior to the initiation of chemotherapy and is continued to 6 months after chemotherapy is finished , as this can prevent developing severe hepatitis. It is necessary to permanently monitor patients so we can detect earlier a reactivation of viral infections. In the presented case, in the period of biological therapy the patient suffers from hepatitis reactivation with VHB, a change of the chemotherapy regimen being required.

THE MANAGEMENT OF A REFRACTORY MULTIPLE MYELOMA CASE.

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Introduction. Multiple myeloma represents a malignant clonal proliferation, of unknown origin of the plasma cells from the bone marrow. The etiology is unknown, but the myeloma biology suggests a stepwise process, consisting of genetic abnormalities at the level of immunoglobulin genes, having as result the activation of the oncogenes with the trigger of the uncontrolled proliferation of plasma cells. The disease diagnosis depends of the abnormal plasma cells identification at the bone marrow level, of the serum and urine M protein and of the bone lesions.
Case report. We present the case of a 49 years old patient, diagnosed with multiple myeloma with light Lambada chains, in October 2010. The patient was hospitalized in County Hospital of Resita, for intense chest pains. The routine biological investigations reveal anemia (Hb =9.7 g / dL), inflammatory syndrome (ESR = 108 mm / h) and azotate retention. Subsequently, serum protein electrophoresis and serum protein immunoelectrophoresis, which highlights the presence of a monoclonal band for lambada light chains, is performed.
The patient is directed to the Hematology Department of Timisoara for further investigations and specialized therapeutic conduct. The bone marrow cytology has highlighted the presence of the plasma cell infiltration in proportion of 31 %, raising suspicion of multiple myeloma, subsequently confirmed on the basis of BOM.
The radiological investigations (skull, spine, chest, pelvis radiography) have highlighted osteolysis areas, with 2 cm diameter at the parietal bone, incipient coxartrosis changes. Based on the clinical and paraclinical investigations, is established the diagnosis of stage II ISS multiple myeloma with Lambada light chains. It was established Alkeran and Dexamethasone therapy and 4 applications were performed, obtaining a partial response (plasma cell infiltrate 12,5 %).
Subsequently, a second therapy line with Velcade in combination with Dexamethasone and Caelyx is established. 8 applications were applied, well tolerated, obtaining complete remission (BOM without plasma cell infiltration). Subsequently, maintenance treatment is performed with Thalidomida 200 mg / day (.3.2012-10.2012), followed by Roferon 23 x 1 MU / week (11.2012-02.2016). Treatment with Roferon 3 x 1 MU / week is recommended.
At the March 2016 reevaluation, relapse of the disease is detected and the third line of chemotherapy with Velacade in combination with Dexamethasone is initiated, well tolerated until present.
Conclusions. Both disease evolution and prognosis are marked by the refractory character to treatment. After the multiple therapeutic schemes approached, the combination Velcade + Dexamethasone + Caelyx has been proved to be the most efficient, contributing to induce a complete answer but short term, to the present case (5 years).

THERAPEUTIC MANAGEMENT AND EVOLUTION OF A PATIENT DIAGNOSED WITH MDS-MPNs IN EVOLUTION.

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Introduction. Myelodysplastic Syndromes are a group of diseases caused by clonal proliferation of abnormal pluripotent stem cells, clone malignancy causing gradual replacement of normal hematopoiesis, resulting in quantitative and qualitative hematopoietic abnormalities with cytopenia on one or more cell lines from the peripheral blood level, in conditions in which the bone marrow stays normal or even hypercellular while a myeloproliferative syndrome is characterized by a proliferation of mature cells morphologically and functionally normal in the bone marrow.
Case report. We present a patient aged 77 years, retired, from urban areas, without a personal history of pathological material, who is investigated in 01.2013 in the hospital of Resita with altered general state, asthenia, fatigue, dizziness, skin pallor, without lymphadenopathy superficially palpable, without organomegaly, balanced cardio-respiratory arrest and he was diagnosed with sideroblastic anemia for which he received MER transfusions. The patient was subsequently hospitalized in the Hematology Clinic in Timisoara to carry out further investigations and conduct specialized therapeutics.
Routine biological investigations reveal a moderate normochromic anemia (Hb = 8g / dL) and thrombocytosis (platelets = 700,000 mm3). The bone marrow aspirate raise suspicion of a syndrome 5q- SMD type. A cytogenetic examination is performed and it revealed no chromosomal aberations. He was further investigated with colonoscopy: Biopsy reveals benign sigmoid colon polyps, gastroscopy: apparently normal, gynecological examination: look normal, abdominal ultrasound: apparently normal, chest radiograph: apparently normal mammogram: normal appearance.
Based on CBC, marrow aspirate and cytogenetic examination a MDS-MPNs diagnosis is established and blood substitution and iron chelation therapy is periodically administrated. It is also initiated treatment with Hydrea but the patient does not tolerate it and after that, treatment with Thromboreductin is initiated, with a low compliance from the patient as the doses administered are not as recommended.
The therapeutic objectives are maintaining the Hb levels between 10 and 12 g / dL, decreasing transfusion requirements, normalizing platelet count, increase the interval between hospitalizations and maintaining a satisfactory quality of life.
Currently the patient is taking Thromboreductin, Erythropoietin, iron chelation therapy (Exjade) and blood transfusions required at 4-6 weeks.
Conclusions. Regarding of the low compliance of the patient to treatment and need for monthly hospitalizations for administrating blood substitution therapy, the patient's quality of life remains satisfactory with the possibility of carrying out normal daily life activities. In terms of diagnosis, evolution is toward LA (both SMD and the SMPc). The prognosis is reserved because thrombotic / thromboembolic complications can occur due to the increased number of platelets as well as complications related to organ failure due to iron overload.

THE EVOLUTION OF PATIENTS WITH OSTEOMYELOFIBROSIS IN THE CLINIC OF HAEMATOLOGY AND BONE MARROW TRANSPLANT TÂRGU MURES.

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Introduction. Myeloid metaplasia with myelofibrosis (MMM) is a clonal neoplastic disorder of hematopoietic stem cells, which is part of the chronic myeloproliferative diseases along with Polycythemia vera, essential Thrombocytosis and chronic myelogenous leukemia; resulting in bone marrow insufficiency or acute leukemia. MMM is the most rare entity in the group of myeloprolieferative neoplasms. It can be de novo or secondary myeloid metaplasia post polycythemia vera or post essential thrombocytosis. MMM is characterized by the coexistence of the three fundamental cytological disorders: clonal proliferation of hematopoietic stem cells in the bone marrow, reactive proliferation of the stromal cells (fibroblasts and osteoblasts), which results in myelofibrosis and extramedullary haematopoiesis in the spleen, liver and other organs. Extramedullary hematopoiesis may cause symptoms, depending on the organ or site of involvement (hepatomegaly, splenomegaly). The V617F mutation to the JAK2 protein can be found in majority of patients with primary myelofibrosis. For a long time the treatment of MMM was focused only on palliative, symptomatic treatment. In November 2011 ruxolitinib was approved as a treatment for primary or secondary myelofibrosis. Ruxolitinib serves as an inhibitor of JAK 1 and 2, which significantly reduces spleen volume and decrease the symptoms of myelofibrosis.
Material and methods. We present the experience of

Hematology and Bone Marrow Transplantation Clinic in of Targu Mures by evaluating the efficiency and tolerance to treatment with JAK inhibitors in patients diagnosed with MMM. Results We evaluated 14 patients diagnosed with primary or secondary MMM treated with Ruxolitinib in our Clinic. We analyzed clinical and biological parameters at diagnosis, at initiation of therapy and monthly.
We evaluated the therapeutic response by measuring the size of the spleen at diagnosis, then monthly during the treatment. We observed decreased spleen size in the majority of our patients, decreased transfusion necessity. Only 2 cases were found with severe anemia, where blood transfusion was necessary. In one patient also severe thrombocytopenia was associated, which required stopping the treatment with Ruxolitinib after 6 months of dosing.
Conclusion. In our study the Ruxolitinib therapy was effective in most patients with MMM by decreasing spleen size. The accurate monitoring of these patients it is important to control the hematological disorders such as anemia and thrombocytopenia.

QUALITY OF LIFE OF PATIENTS WITH MALIGNANT HEMOPATHIES COMPARED TO GENERAL POPULATION.

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Introduction: Quality of life is a qualitative measure of an individual general status very hard to cuantify, but very important for overall functional status.
Purpose: In the present study, we try to find correlations between areas of life which are most affected by hematological malignancies and its degree of impairment by comparing with the general population. This study does not undertake an exhaustive study of quality of life, furthermore it's a starting direction for future subsequent studies.
Method: In order to compare patients with hematological malignancies with the general population we used a quality of life questionnaire WHOQOL-BREF1 - all rights reserved. The study was conducted from June to July 2016, and the first group of subjects comes from Coltea Hematology Clinic. All patients included in the first group have at least 6 months since the diagnosis. WHOQOL-BREF1 test is divided into four domains: Physical Health, Psychological , Social Relationships, Environment. The first group of patients with hematological malignancies includes 70 people with an average age of 61.45 years with a distribution by diseases, as follows: Non-Hodgkin's lymphoma (NHL) - 21 subjects, Multiple Myeloma (MM) - 15 subjects, Myelodysplastic Syndrome (MDS) - 7 subjects, Acute myeloid leukemia (AML) - six subjects, Chronic Lymphocytic Leukemia (CLL) – 6 subjects, Hodgkin Lymphoma (HL) - 4 subjects, Myeloid metaplasia with myelofibrosis (MMM) – 4 subjects, Essential thrombocythemia (ET) - 3 subjects, Chronic myelogenous Leukemia (CML) - 2 subjects, Waldenstrom's disease - 1 subject, Acute Lymphoblastic Leukemia (ALL) - 1 subject. The second group is the control group and includes 71 subjects with an average age of 49.30 years. For subjects in the second group, impaired health is mainly of cardiovascular origin. Also in this group were not included subjects with other oncological pathology.
Results: The responses to the questions were grouped into the 4 mentioned domains and further processed by suggested calculation by questionnaire WHOQOL-BREF. Regarding domain 'Physical Health' in patients group it was obtained a value of 51.4244 ± 18.5465, while in the control group the value was 68.1298 ±20.5018, with statistic significance (P<0.0001). In 'Psychological' domain values were: 70.0581 ± 13.6701 - patients, 73.8262 ± 17.6941 - general population (P> 0.005). Regarding 'Social relationships' there were obtained the following values: 65.715 ± 15.4466 – patients, 69.9536 ± 17.8443 - general population (P>0.05) and in the domain of 'Environment': 63.1225 ± 13.1145 - patients, 62.9376 ± 14.4203 - the control group (P> 0.05). There's a difference between the two groups in the 'Physical Health' domain (ability to perform daily living activities), meaning a lower physical health in the first group, while in the remaining domains there aren`t any significant differences. There are also some differences in the first group in the same domain of physical health among patients with NHL (54.5413 ± 16.7213) and patients with MM (44.0426 ± 21.2434) - MM patients have a greater impairment of physical health, but without statistical significance (P = 0.12). The 'Physical Health' domain includes questions about: physical pain, need of medical treatment, exercise capacity, ability to handle daily living activities, quality of sleep.
Conclusions: The study found that 'Physical Health' is the most affected and patients with hematological malignancies feel mainly a deterioration in physical performance, other domains are not as affected.
The 'Physical Health' domain, by being the most affected, it is important to focus on the best achiveable physical status of patients with hematologic malignancies, for example by promoting regular

physical activity.
These results are subject to a limited number of patients and the data collection was performed in a short period of time, so for a better highlight concerning the differences between the two groups, it requires a longer period of time and a greater number of patients in order of having a statistical significance.
Also, based on this study, we can not exclude differences that may occur in other areas between the two groups.
1.Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. (1998) Psychol Med, 28(3), 551-558.

PROGNOSTIC IMPLICATIONS OF THERAPEUTIC RESPONSE IN ALL.

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Introduction: Acute lymphoblastic leukemia (ALL) encompasses a range of clonal hematologic diseases with their origin in the lymphoid progenitor cell, having a heterogenous way of clinical presentation and evolution. Risk stratification both at onset and during therapy remains the cornerstone of individualized treatment. Prognostic factors for patients diagnosed with ALL can be broadly divided into two categories: those present at diagnosis and those identified by monitoring the pacient during or post-treatment. In the last two decades, modern investigations like cytogenetics and molecular biology have surpassed clasical prognostoc factors, leading to a „changing paradigme" in terms of risk stratification, from a historical approach based on age, sex, number of circulating leukocytes and morphological analysis to a more recent and powerful that includes dynamic immunophenotype, cytogenetic analysis and molecular markers evaluation (Rowe, 2010). In recent years, minimal residual disease (MRD) has been recognised as a significant indicator of short and long term evolution, both in the pediatric category (Cave et al. 1998) and in the adult.
Purpose: This study aims to highlight the importance of a reliable assessing of treatment response in order to choose an optimal therapeutic attitude, based on both theoretical and practical considerations.
Method: In this paper was carried out a comparative dinamic analysis of tho cases of acute lymfoblastic leukemia. It was followed the response to treatment by methods available in the Coltea Hematology Clinic (morphological and flow cytometric analysis.
Results: We have followed two cases of acute lymphoblastic leukemia with the same prognostic value at onset, whose response to treatment monitoring has detected different evolutions. For the case with early relapse was adopted a reinduction scheme obtaining a second remission and for the latter to continue consolidation treatment with maintenance of remission.
Conclusions: The presented cases illustrate important prognostic value of therapeutic response. The methods of assessment the treatment response for a deeply sensitive result still raises standardization, accessibility and cost issues. A profound diagnostic approach of complete remission, early relapse or lack of response to standard therapy provides information to individualized care.

PROCOAGULANT STATUS - PRENATAL MORBIDITY AND MORTALITY IMPLICATIONS

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Introduction: The existence of an anormaly in coagulation fibrinolytic system prone to triggering thrombotic process. Our study aims to counseling the patient about preventing the thrombotic process, hypercoagulable phenomena in the deep venous system and placental , and also the prevention of embolic potential .
Material and methods: presenting the case of patient TG: IVG0P treated with Clexane 0.6 IU / day with favorable evolution , 32 years old , 3 pregnancies stopped in evolution previously, located in Municipal Hospital Filantropia, whom were performed clinical evaluations , according to the job of observation and laboratory - molecular techniques (Real-Time PCR , sequencing) Blood tests and imaging exploration .
Results: profile negative antiphospholipid syndrome , factor V Leiden negative mutation , prothrobin negative mutation (factor II) , C677T mutation genotype homozygous, 675 polymorphism 4G/5G-genotype homozygouse (status 4G/4G mutant type) , kayotype 46, XX, 9qh+. Status homozygous for mutation C677T may result in increased plasma levels of homocysteine , especially at patients with folate and vitamins level decreased in group B. Hyperhomocysteinemia is a risk factor for arterial thrombosis , venous and miscarriage , so all previous studies recommend normalization of homocysteine through vitamin adequate replacement and periodic control of homocisteinemiei .
Associated risk factors such as immobilisation , trauma ,

surgery , pregnancy, smoking, obesity , use of oral contraceptives can lead to a marked predisposition latromboza . Be warned about the mutation importance as a risk factor for coronary diseases , myocardial infarction and preeclampsia. Homozygous status for the deletion of PAI -1 gene promoter (status 4G / 4G mutant type) favors preeclampsia at pregnant women . Guanosine deletion in position 675 PAI -1 gene lead to increased levels of PAI -1 in blood , being a risk factor for thromboembolic disease. Maternal genetic analysis report identifies a secondary constriction at the elongated long arm of chromosome 9 - polymorphisms with normal karyotype 46 , XX , + 9qh , while paternal chromosomal map does not indicate the number or structure abnormalities - 46, XY .

Conclusion : Linking hypercoagulable status with genotyping results and applying preventive therapy , aimed at prevention of intravascular thrombosis with serious consequences .

JAK2 V617F POSITIVE POLYCYTHEMIA VERA AFTER FOUR YEARS OF STABLE CHRONIC MYELOGENOUS LEUKEMIA IN COMPLETE MOLECULAR REMISSION UNDER IMATINIB TREATMENT. CASE REPORT.

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Background. In 1951 Dameshek described for the first time the concept of chronic myeloproliferative syndromes. These conditions included CML and the current classical BCR-ABL-negative MPNs, represented PV, ET and PMF. CML is currently separated from the rest of MPNs due to its distinct cytogenetic and molecular characteristics. However, CML shares some common features with MPNs. The literature reports rare cases of patients with both BCR-ABL rearrangement and JAK2-V617F mutation as evolution of CML. Materials and **Methods**. A 51-year old man was diagnosed in 2009 with Ph + CML. At diagnosis, a mild anemia and a reduced number of erythroblasts in the bone marrow were present. He was started on Imatinib. After 12 months a MMR and at 18 months a CCR were reached. Starting in 2013 the patient began to present pruritus and erythema. A hemogram showed elevated levels of hemoglobin, hematocrit, red blood cell counts and mild leucocytosis and thrombocytosis. Molecular studies detected the presence of JAK 2 homozygous mutation. Bone marrow panhyperplasia and increased LAP score were also noted. Results. A PV-associated CML was diagnosed. Low dose Hydrea and occasional phlebotomy to keep the Ht <45% were added to Imatinib. At the last evaluation (June 2016), the patient was maintained BCR ABL negative (RMC). Discussions. The combination of two molecular markers characteristic for two myeloproliferative neoplasms is rare but not impossible and such situations have already been described in the literature. In most cases JAK 2 mutation occurred when the BCR-ABL malignant clone was suppressed by tyrosine kinase inhibitors, which advocates two independent mechanisms of aberrant stem cell clonal growth, probably in a genetic instability background. Also, Kralovics believes that the JAK2-V617F mutation could represent a genetic defect occurring later in the progression of the CML. In addition, simultaneous occurrence of BCR-ABL and JAK2-V617F (before any treatment) cases and BCR-ABL+ CML cases that occurred as progression of a JAK2 + PV were also described. Conclusions. Further studies are needed to discover the causes, clinical and evolutive implications as well as the most appropriate treatment for these particular situations.

THE ROLE OF IMMUNOPHENOTYPING BY MULTIPARAMETRIC FLOW CYTOMETRY IN DIAGNOSIS OF MIXED PHENOTYPE ACUTE LEUKEMIA.

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INTRODUCTION

The majority of acute leukemias (AL) can be classified as myeloid, B, or T lymphoid. In some cases this is not possible because of the evidence of expression of both lymphoid and myeloid lineage-specific antigens in the blast cells. These cases were defined previous as biphenotypic or biclonal AL by EGIL classification. Based on the classification of WHO (2008) biphenotypic and biclonal AL were redefined as the mixed phenotype acute leukemia (MPAL) assigning new criteria for this group of diseases. The purpose of this study was to compare EGIL and WHO (2008) classifications of MPAL and to present importance of immunophenotyping by multiparametric flow

cytometry in their diagnosis.

MATERIAL AND METHOD

In our report we present 12 cases diagnosed initially with biphenotypic acute leukemia from a total of 272 acute leukemia patients. We performed immunophenotyping of bone marrow samples. Four-color immunofluorescence staining was used. The initial diagnosis was established according to EGIL classification. The same cases were reviewed according to WHO criteria for mixed phenotype acute leukemia.

RESULTS

Based on GEIL scoring system, immunophenotypic analysis identified 8 cases of biphenotypic acute leukemia with B-lymphoid + myeloid lineage, 3 cases with myeloid and T-lymphoid lineage + 1 case of B+T lymphoid lineage. One patient was diagnosed with biclonal AL, both morphologically and immunologically two distinct population of blasts were identified, one with B lymphoid lineage and one with myeloid lineage. After reviewing these cases, in one case (previously diagnosed as biphenotypic acute leukemia with B-lymphoid and myeloid lineage) did not fulfill the diagnostic criteria of WHO for MPAL. The final diagnosis in this case was AML with aberrant lymphoid markers. The other 11 cases were defined as MPAL according to WHO 2008 criteria.

CONCLUSION

By applying the WHO 2008 criteria, much stricter than the previous classification of EGIL, we can avoid overestimation of biphenotypic AL, some of them being redefined as ALL with aberrant myeloid markers or AML with aberrant lymphoid markers. This has particular implications for the choice of therapeutic strategy in patients with MPAL.

HODGKIN'S DISEASE PROGNOSTIC FACTORS-MALE PACIENTS IN TWO AGE GROUPS.

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Introduction. Hodgkin's disease is a malignant proliferation of lymphoid tissue , is described for the first time in 1832. In general, this disease affects young people , if the disease is detected early and treated properly, patients can lead a normal life .

Scope. Clinical Study proposes positive or negative prognostic factors present in patients of the same sex and about the same age .

Methods. We conducted a retrospective observational analytical study on a two-year period , between 01.2008 and 12.2010 , on a sample of 54 patients, known Hematology Clinic Timisoara with Hodgkin's disease . Criteria for inclusion in the study were male , aged 20-40 and 41 - over 65, who are in first-line chemotherapy , ABVD protocol . The variables in this study were the presence or absence of bulky lymph nodes debut, the advanced stage of disease (grade IV B) onset, histologic form , cardiovascular and respiratory comorbidities associated, infectious complications after chemotherapy , elevated LDH and VSH .

Results. The patients were divided into two age groups with an average age of 31 years in the first group (Group1) and 57, in the second group (grup2). Of the 21 patients in Group1, negativ prognosis factors were advanced stage of disease onset 38%, infectious complications of respiratory post chemotherapy onset 25% and positive factors were histological BH with SN more common in young people and therapeutic response good after the second, third application ABVD (67%). In grup2 negativ prognosis factors was associated comorbidities (CIC HTAE, HTP, COPD), haematological and respiratory infectious complications after chemotherapy (> 50%) with secundary anemia and neutropenia , elevated VSH and LDH (12%) and therapeutic response poorly to treatment protocols (66%).

Conclusions . Positive or negative prognostic factors are different depending on the age group , although young patients with BH , as with nodular sclerosis have a good prognosis , with cure rates of 60-80% of them, they have early relapsed disease (before 12 months), while patients of grup2 harder respond to chemotherapeutic protocol but they presentis longer lasting remission .

DOUBLE AUTOLOGOUS STEM CELL TRANSPLANTATION IN CASE OF A PATIENT A MULTIPLE MYELOMA AND PLASMOCITOMA.

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In our study is presented a case of a 41 year old patient diagnosed in 01.2015 with non-secretory multiple myeloma, treated with 3 courses of chemotherapy, followed by stem cell mobilization and harvesting, and

2 more chemotherapy courses. In 06.2015 was performed autologous stem cell transplantation and 6 courses of chemotherapy. The patient received monthly bone remineralization treatment with good evolution until 05.2016, when relapse appeared with sever diffuse skeletal pain and spinal cord compression symptoms. The effected analysis showes the presence of a spinal cord tumor reason why decompressive laminectomy was performed (histopathologic diagnoses: multiple myeloma). Due to the aggressive caracter of the disease after a preliminary conditioning treatment (Melphalan+Busulphan), in 07.2016 the patient underwent the second autologous stem cell transplantation to stabilize the disease progression until an allogeneic transplantation can be performed.

THE RESULTS OF AUTOLOGUS STEM CELL TRANSPLANTATIONS IN HOGKIN LYMPHOMAS PERFORMED IN CLINICAL HEMATOLOGY AND BMT UNIT TG.-MUREŞ.

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Introduction: Autologous stem cell transplant (ASCT) plays an integral role in the treatment of patients with Hodgkin's lymphoma. Most patients with Hodgkin's lymphoma are cured with combination chemotherapy with or without radiation therapy. ASCT is currently the optimal treatment for patients who fail chemotherapy and radiation therapy. Patients who relapse after chemotherapy for Hodgkin's lymphoma are treated with second-line chemotherapy, which is often followed by an ASCT. In the treatment of these patients, the timing of ASCT is important and should not be delayed.
Materials and methods: A retrospective study was performed. The analysis involved 107 classical Hodgkin's lymphoma patients who were consecutively submitted to high-dose chemotherapy followed by autologous transplants in the Bone Marrow Transplantation Unit Tg-Mures between 2006-2015.
Results: 64 males and 43 females with a median age of 35 years (range, 19 to 63 years) received autografts while in complete remission or when they had sensitive disease or resistant disease at a median time of 26 months (range, 4 to 230 months) after diagnosis. All the patients received high-dose chemotherapy without radiation for conditioning. The graft consisted of peripheral blood.
Conclusion: Autologous hematopoietic stem cell transplantation is an effective treatment strategy for early and late relapse in classical Hodgkin's lymphoma for cases that were responsive to pre-transplant chemotherapy. Refractory to treatment is a sign of worse prognosis.

CARDIAC DISEASE IN A PATIENT WITH ACUTE MYELOID LEUKAEMIA DEVELOPED ON A CHRONIC MYELOMONOCYTIC LEUKAEMIA.

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Introduction: Chronic Myelomonocytic Leukaemia is disorder of the pluripotent stem cell the exhibits characteristics of both Myelodisplastic Syndrome and Mieloprolferative neoplasms. Chronic Myelomonicytic Leukaemia is characterised by persistent monocytosis (>1000/mmc), myeloblasis are 5-9% in blood and <20% in bone marrow. Chronic Myelomonocytic Leukaemia has been classified as a Myelodisplastic Syndrome according to FAB classification and more recently WHO classification has placed it as a mixed myelodisplastic/myeloproliferative disease .Symptoms include splenomegaly, aenemia, fever, night sweats, pleural, pericardial effusion. The incidence has been estimated at 1 per 100.000 persons per year with a propensity for the male sex and a medial age of 65-75.
Case presentation: We present the case of a 73 year old female with a history of arterial hypertension, who in july 2015 was admitted with fever, splenomegaly, weight loss; blood work showing leucocytosis (26.960/mmc) with neutrophilia (12.250mmc) and monocytosis (10.740/mmc). Bone marrow aspiration corroborated with peripheral blood abnormalities lead the diagnostic to a borderline Chronic Myelomonocytic Leukaemia-Acute Myeloblastic Leukaemia with myelodisplastic characteristics (Acute Myeloblastic Leukaemia post Myelodisplastic Syndrome/Myelo-proliferative Neoplasms). Echocardiography showed minimal pericardial effusion and isolated ventricular extrasystole. Cytoreduction therapy with Hydrea was started with periodic hemoleucogram evaluations. In september 2015 during routine evaluation, the patient presented leucocytosis with 52,6% immature monocyte population and thrombocytopenia. Bone marrow

aspiration and immunophenotype confirmed the transformation to acute myelomonicyte leukaemia. Accompanying the transition, the patient also developed 2:1 atrial flutter, and later rapid atrial fibrillation and severe pulmonary hypertension. Once the clinical and hemodynamic symptoms were stabilised, Decitarabine and appropriate cardiac therapy was started resulting in clinical and paraclinical improvement. Haematologicaly, under Decitarabine treatment, the elevated monocytic count (4-1000) persisted for 7 months, before eventually normalising.
Conclusions: Cronic Myelomonicytic Leukaemia is a type of Myelodysplastic Syndrome with 15-55% Acute Myeloblastic Leukaemia transition risk showing both characteristics of Myelodysplastic Syndrome and Myeloproliferative Disorder. With the transition to acute Myeloblastic Lukaemia, the cardiac disfunction is aggravated, needing positive inotrope treatment, beta blocker, calcium blocker, high ceiling diuretic and oxygen therapy. Decitarabine treatment lead to the stabilisation of the cardiac disease and the normalisation of monocyte count. Over the course of treatment , the patient required periodic cardiac function evaluation and the adjusting of cardiac medication.

THROMBOTIC THROMBOCYTOPENIC PURPURA – CASE STUDY.

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Thromobotic thrombocytopenic purpura (TTP) is defined by the existence of thrombocytopenia and microangiopathic haemolytic anemia in the absence of apparent causes. Impaired microvascular and platelet aggregation with the formation of intravascular thrombus represent the initial mechanism of the development of TTP. It manifests itself as a fulminant disease which consists of five essential components, these being microangiopathic haemolytic anemia, thrombocytopenic purpura, neurologic abnormalities, renal disease and fever. The treatment of TTP is considered to be a heamatological emergency, which invokes the swift application of plasmapheresis in association with broad-spectrum antibiotics and corticosteroids. In our paper we would like to present the case of a 34 year old female patient, without any known history of chronic disease, which she was emergently admited in Internal Medicine Clinic 1 - Haematology Tg. Mures, with the suspicion of TTP. The patient arrived in an altered general state, comatose with the GCS of 3 points, pail skin, presenting ecchymosis of the extremities, thoracic petechiaes in the anterior region. The patient is cared for in the intensive care unit, where after a short period she develops left hemiplegia, possiblly the result of cerebral microthromboses, being in a convulsive state with focal left hemicorporal jacksonian crises, nistagmus and bilateral conjunctival bleeding. Looking at the laboratory results, we can find severe thrombocytopaenia (Tr: 24.000-12.000/mmc) and haemolytic anemia(Hb: 6,66g/dl Ht: 19,6-19,4%), the periferic bloodsmear shows a large number of schistocytes, accentuated poikilocytosis and a highly elevated LDH level (LDH:1,360U/l). The patient recieved 10 rounds of plasmapheresis, resulting in the gradual decrease of the LDH level and the slow increase of the number of thrombocytes. The evolution of the patient is favorable, being in a better state looking at the paraclinical results (Hb: 9,9g/dl, Tr: 235000/mmc), clinically presenting a left hemiparesis. At the moment the patient is in the evidence of the Hematology Department 1, and is being responsive to the corticosteroid and plasmapheresis treatment. In conclusion, we insist on the necessity of an early diagnosis and of urgent therapeutic intervention, for a favorable outcome and a better survival, in any cases of TTP.

Key words: *TTP, thrombocytopenia, microangiopathic haemolytic anemia, plasmapheresis.*

HEMATOLOGICAL ABNORMALITIES IN HIV/AIDS INFECTION.

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Introduction. There is a definite association between infection with human immunodeficiency virus (HIV) and various hematologic events , this being recognized since the discovery of HIV. Hematologic abnormalities described in HIV / AIDS are :
1 – cytopenias: the highest frequency has thrombocytopenia , which may be the first sign of HIV infection (10% of cases).
2 – Myelodysplasia
3 – Thrombotic microangiopathy/Thrombotic Thrombocytopenic purpura
4 - The most common hematological malignancies found in HIV / AIDS are: Hodgkin lymphoma and non – Hodgkin esspecialy high aggressive types such as plasmablastic lymphoma, serous type lymphoma, diffuse large B cell lymphoma (DLBCL), cerebral primary lymphoma , Burkitt lymphom or multicentric Castleman disease. Appears at pacients with long evolutive disease and low CD4. In malignancies

ethiopathogenesis are directly involved also Ebstein-Barr virus, Cytomegalovirus, HHV8 (Herpesvirus – 8). The treatment is the combination of specific HIV treatment (Highly Active Anti Retroviral Therapy – HAART) and chemotherapy (standard type CHOP regimens or aggressive like CODOX -M / IVAC , DA-EPOCH). The mortality rate is high and evolution is compounded by complications , especially opportunistic infections .

Materials and methods: In the Hematologic department of Fundeni Clinica Institute there were hospitalized between 2011-2016, 33 patients, 18 men and 15 women, of which 6 were known with HIV/AIDS. There were no datas whether they were receiving antiretroviral treatment at the time; 26 patients were diagnosed with HIV/AIDS simultaneously with hematologic disease .

Results:18 pacients were men and 15 were women.

The age was between 18 and 71 years old (the median age was 43,69).

16 pacient (48,48%) were diagnosted with lymphoproliferative disorders – 3 pacient with Hodgkin Lymphoma, 13 with various types of non – Hodgkin lymphomas: 8 cases of diffuse large B – cell lymphoma, 2 with small B cell type from witch one is marginal zone lymphoma (MZL), Burkitt lymphoma – 2 cases and one with Adult T – cell lymphoma (ATLL) with Human T-cell lymphotropic virus (HTLV). Other malignancies dicovered were: one case of multiple myeloma IgA k type, IIIA stage , one case of acute lymphoblastic leukemia and one case of myelodysplastic syndrome secondary HIV. The other 14 patients showed nonspecific changes in the blood : anemia through different mechanisms (folate deficiency , chronic simple anemia, iron deficiency), thrombocytopenia, agranulocytosis .

26 subjects (78,78%) had concomitant discovery of HIV and the hematological changes. Coinfections found in these subjects were: hepatitis B virus , hepatitis C virus , Epstein Barr virus , Cytomegalovirus , HTLV , Pneumocystis jiroveci.

The treatment options chosen were regimens like ABVD for Hodgkin lymphoma, R/CHOP for DLBCL, HyperCVAD for Burkitt lymphoma. Simultaneously they received specific therapy (HAART.)

On the 1th of July, from the 33 pacients analised and diagnosted with HIV/AIDS, 14 pacient witch had hematological manifestations such as cytopenia/ myelodysplasia were lost from evidence, being guided to an infectious diseases department for specific treatment. Of the 19 patients who were diagnosed with hematologic malignancies and HIV infection, 7 patients died of infectious complications after chemotherapy . It is mentioned that a patient with MZL is in complete remission after CHOP and splenectomy.

Conclusions: Hematologic abnormalities, particularly cytopenias, may occur in HIV infection since the disease onset (primary infection) or in advanced stages. HAART is recommended to start immediately after HIV infection is diagnosed, with the possibility of total or partial correction of cytopenias. It is mandatory to be associated chemotherapy in order to control viral infection and decrease the risk of opportunistic infection. Although lately there have been advances in antiretroviral therapy, the mortality in hematologic malignancies associated with HIV/AIDS remains high (average survival is between 1 and 3 years, depending on the histopathological type of the malignancy, the regimen chosen or sensitivity to HAART).

AN ATYPICAL COURSE FOR A MARGINAL ZONE LYMPHOMA – CASE REPORT.

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Background: Splenic marginal zone lymphoma is characterized in medical papers as an indolent lymphoma, even in the advanced stages. The tumour usually affects the spleen, splenic hilar lymph nodes, bone marrow and peripheral blood, whereas the peripheral lymph nodes are not typically affected. Transformation into a large B cell lymphoma is very rare for this type of lymphoma, as borne out by the very infrequent reports in medical papers. Case report: We present below the case of a 63 year old man who was referred to our department presenting enlarged peripheral lymph nodes and splenomegaly. Blood samples revealed leukocytosis (WBC 56.8 x 109 /L) with 88% pleomorphic lymphocytes, mild thrombocytopenia (80x 109 /L) and a high LDH serum value. The diagnosis of B-cell marginal zone lymphoma was established on the basis of flowcytometric analysis of the peripheral blood and histopathological and immunohistochemical examination of the lymph node biopsy. The tumor cells were small/medium-sized, positive for CD20, CD79a and negative for CD3, CD5, CD23, CD10, BCL6, Cyclin D1 and SOX11. After an initial good evolution with R-CHOP regimen, the patient presented a quickly expanding tumor mass in the right pectoral region before the fourth course of chemotherapy, associated with pain and collateral circulation at this level and swelling of the right arm. In response we performed another biopsy. The histopathological and immunohistochemical examination established the diagnosis of a blastic variant marginal zone lymphoma, while the

flowcytometric analysis of the peripheral blood revealed a clonal, heterogenous proliferation: one with the same CD5-CD23-immunophenotype as in the initial diagnosis, but also a CD5+ C23- population (mantle cell immunophenotype). Under DHAP salvage chemotherapy, the outcome was rapidly unfavorable, with tumor enlargement, CNS involvement and an overall survival of 6 months from the diagnosis.

Conclusion: Although splenic marginal zone lymphoma is known as an indolent lymphoma, it can also develop aggressively. An aggressive course may be suggested by the clinical behaviour (peripheral adenopathies at the onset), by the histopathological exam (i.e. blastoid appearance of the tumor cells) and by the immunophenotype of the tumor cells (mantle cell CD5+ C23- immunophenotype). Histologic transformation is rare compared to the rest of the entities included in the same indolent category, but can occur early in the course of the disease.

SUBCLINICAL CARDIAC DYSFUNCTION IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA.

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INTRODUCTION: Acute lymphoblastic leukaemia (ALL) is the most common malignancy in childhood. Among the most frequently used chemotherapic drugs in standard treatment of this pathology are the anthracyclines, which are known for their potential cardiotoxicity, clinically manifested by myocardial contractility dysfunction and/or abnormal heart rhythms. It is recommended not to exceed an anthracycline cumulative dose of 450-550mg/m2. Within the BFM-ALL IC 2002 protocol, it is used a maximum dose of 240mg/m2, for standard and intermediate risk, and of 300mg/m2, in patients with high risk.

OBJECTIVE: to evaluate myocardial contractile and diastolic functions in paediatric patients diagnosed with ALL and treated according to standard chemotherapic protocol

MATERIALS AND METHODS: Between February 2015 and August 2016, 54 patients, over one year old, were diagnosed with ALL in our Department, based on peripheral blood smear, bone marrow aspirate, cytogenetics, immunophenotyping and molecular biology. The family members of 5 patients refused participating in the study, 2 children were excluded due to atypical morphology (mature B cell and bilinear leukaemia), 6 patients died during treatment. A complete echocardiological examination was performed, including Tissue Doppler Imaging (TDI), to all patients at diagnosis, after 6 months (after the entire anthracycline dose was administrated) and at one year after the diagnosis (approximately 6 months after the last doxorubicin dose). We evaluated both global systolic function parameters (ejection fraction-FE in M mode, left ventricular outflow tract-VTI/LVOT), and diastolic function parameters (early filling velocity-E, late filling velocity-A, deceleration time-TDE, isovolumic relaxation time -TRIV), but also longitudinal contractility in lateral wall of right ventricle (S'VD), septal wall of left ventricle (S'S) and lateral wall in left ventricle (S'L). We compared the values obtained at all three evaluations, and the results were analysed with SPSS Statistics 17, by performing t-test, considering $p<0.05$ to have statistical significance.

RESULTS: Of the 54 patients diagnosed, 41 are presently in the study, 19 of them were evaluated by echocardiography in all three visits: at diagnosis (V1), at 6 months (V2), at 1 year (V3). Of these 19 patients: 8 F and 11 M; age groups: 12 patients 1-5 years, 7 patients 6-15 years. Based on immunophenotyping analysis, 3 children presented with T cell lymph oblasts, the other 16 with B cells lymphoblasts. 8 patients (42%) expressed TEL-AML1 fusion gene and 1 patient E2A-PBX1. The majority had a good prednisone response; only 1 remained with more than 1000 blasts/microl in day 8, being appointed to high risk group.

Between the parameters for global systolic function, FE was not altered statistically significant, while VTI/LVOT dropped at V2 (p=0,005), increasing at V3 (p=0,001). Diastolic dysfunction was shown by the decline in E and TRIV values at V2 (p=0,001, respectively p=0,075-marginal significance) with the return to initial value at V3 (p=0,014, respectively p=0,017). The alteration in TDE and A values were not statistically significant. TDI parameters showed a longitudinal contractile dysfunction by decreased S'L value (p=0,011), S'S (p=0,001) and S'VD (p=0,001) at V2, diminution which is maintained at V3 (p=0,004, p=0,002, respectively p=0,001).

CONCLUSIONS: Due to known anthacycline cardiotoxicity, it is mandatory for patients to benefit from an echocardiological evaluation before initiating chemotherapy and also during the treatment. We revealed a transiently diastolic dysfunction, shown by transmitral diastolic flow, to identifying patients at risk for developing heart damage during treatment for ALL, but also amongst long-term survivors. Due to the

extraordinary ability of the heart to adapt, even small changes in cardiac function can be sign of heart impairment. Presently, echocardiography is considered the gold standard for diagnosing cardiotoxicity. Even though in children's protocols the anthracycline cumulative dose does not exceed the recommendations, we found different grades of systolic and/or diastolic dysfunction in most of our paediatric patients. Subclinical damage is difficult to show using standard methods, more sensitive techniques being needed, such as TDI and speckle tracking, in order to reveal subtle dysfunctions. Taking into account that a diagnostic protocol for cardiac impairment and follow-up schedule for these patients are not available at the moment, further clinical studies are paramount.

CEREBRAL SINOVENOUS THROMBOSIS IN CHILDREN – CLINICAL MANIFESTATIONS, NEUROIMAGING ASPECTS, RISK FACTORS, TREATMENT, COMPLICATIONS, OUTCOME.

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Introduction. Cerebral sinovenous thrombosis (CSVT) in children are rare (Orphanet 329217, incidence 0.34-0.67/100.000 children/year), possibly fatal (3-12%) diseases, associated with adverse outcomes in > 50% cases, and most probably under-diagnosed (nonspecific early clinical manifestations, low index of suspicion, inadequate neuroimaging techniques). CSVT have a multifactorial etiology: genetic risk factors (congenital thrombophilia) combined with acquired conditions (up to 95% cases). CSVT is increasingly diagnosed in children due to the continuous improvement of neuroimaging techniques. Management remains controversial.

Material and methods. Between March 2012 and April 2014, 6 children aged 10 months to 10 years, 5:1 males/females, none with major chronic conditions, were diagnosed with CSVT in our hospital. All the cases were carefully investigated: personal and family history, clinical manifestations, neuroimaging aspects, congenital and acquired risk factors, treatment, complications, outcome; in the multidisciplinary approach imposed by the complexity of cases, neuroimaging was essential for both diagnosis and monitoring the evolution.

Results. CSVT was associated with infections in 5/6 cases (bronchitis, pneumonia, diarrhea, endomyocarditis, otomastoiditis). In infant and toddlers the initial manifestations were nonspecific (vomiting, lack of appetite, lethargy), followed by seizures (2/6), and coma (3/6); all these had severe iron deficiency anemia (Hb 5.8-7.7 g/dL), and severe dehydration; one patient (8 years) had ocular disturbance after an episode of otitis media, and another (10 years), vomiting, headache, and vertigo after head trauma; both had neglected chronic adenoids , tonsillitis and multiple dental cavities. The limited accessibility/low addressability to medical services should be considered risk factors for the appearance of CSVT and late diagnosis. A genetic predisposition for thrombosis was revealed by the family history (spontaneous abortions, death at young ages, myocardial infarction, stroke, familial hypercholesterolemia in 4/6 cases), the positive genetic profile (all patients had 2-4 risk factors: MTHFR C677T/A1298C; hyperhomocysteinemia; PAI-1 4G, EPCR A3), increased FVIII levels and thrombocytosis in young patients, and internal jugular vein and dural venous sinuses hypoplasia in older patients (10/14 years). The diagnosis of CSVT was established through cerebral CT scan/MRI, 1-3 days (3/6) or later, at 7-14 days (3/6) after the onset; respectively in 24 hours (3/6), 2-3 days (2/6), and 10 days (1/6) from admission; RMIANGIO-RMI (5/6, initially or after CT) was superior to CT scan for the evaluation of thrombosis extension and parenchymal complications. All small children (4/6) had extensive superficial and profound thrombosis at diagnosis, with parenchymal venous/hemorrhagic infarctions (thalamus, internal capsule, corpus callosum, frontal or temporal lobes). In the patient with preceding otitis media (8 years), only the extension of superficial thrombosis to the cavernous sinus (even if not evident >14 days after the onset) could explain the ocular manifestations and pituitary hypotrophy; in the patient with preceding head trauma (10 years), the superficial cerebral vein thrombosis complicated with cerebellar veins congestion explains the cerebellar symptoms. Emergency treatments included: IV rehydration, antipyretic agents, antibiotics, RBCs transfusions, mannitol, dexamethasone, anticonvulsant drugs. Anticoagulant treatment was applied in all cases. Unfractionated heparin (UFH) was initially administered in 4/6 cases for 9-28 days, IV (boluses and continuous infusion);

despite the careful monitoring through APTT, continuous infusion with higher than generally recommended doses (median 26,5 U/kg/h) and repeated IV boluses, APTT was frequently under the optimal therapeutic range (60-85 sec.), with important variations (up to 5-7 the normal range); one patient had extended subdural hematoma after 9 days of UFH. Low molecular weight heparin (LMWH, enoxaparin, dalteparin) was used after UFH discontinuation (4/6 cases) with variable durations, depending on evolution and compliance (30 days, 2 ½, 5 ½, and respectively 6/10/6 months), and from the beginning in 2/6 cases (12-14 days); the residual anti-Xa activity was concordant with the curative/prophylactic regimens in 5/6 cases. Two patients (1½, and 10½ years) were discharged against medical advice, in good state, after 12-14 days of treatment with LMWH (started late after 10-11 days of admission); one infant (aged 10 months at diagnosis) treated with UFH from the 2nd day of admission, had a slow but good evolution; after 28 days of UFH he received LMWH for at least one month; no other data regarding these patients were available. Among the other patients, followed-up for long periods, the two toddlers (1½-2½ years at diagnosis, actual age 5½ years), both treated early (1-2 days after the onset) with UFH (9-14 days), followed by LMWH (10/10/6 months with pauses, respectively 2½ months), had unfavourable outcomes: chronic cerebral thromboses, chronic thalamic infarction, extensive gliosis, hydrocephalus, cerebral atrophy; symptomatic epilepsy, hemiparesis, autism, language disorders; the patient (8½ years at diagnosis, actual age 11 years) with cavernous sinus thrombosis and hypophysis hypotrophy, although late treated with UFH (at least 14 days after the onset) for 15 days, followed by LMWH for 5½ months, had a slow good evolution, with total disappearance of the ocular manifestations and no need for substitution after 5 months of treatment for hypopituitarism.
Conclusions. CSVT in children is a rare disease, most probably neglected in many cases, with challenging diagnostic problems and still unclear therapeutic indications, potentially fatal and with a major risk for long-term sequelae. Treatment of iron deficiency anemia, avoiding dehydration, and correction of chronic ENT problems, could be efficient methods for the prevention of CSVT in children. An early diagnosis based on a high index of suspicion, with neuroimaging in all cases of recent neurologic manifestations, together with the promptly instituted and prolonged anticoagulant treatment could reduce both early complications and long-term sequelae.

Key words: cerebral sinovenous thrombosis, children

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME – SEVERE COMPLICATION OF INDUCTION TREATMENT FOR ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN (PRESENTATION OF TWO CONSECUTIVE CASES).

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Introduction. Posterior reversible encephalopathy syndrome (PRES) in children with malignancy is increasingly recognized in the last years, due to more frequent use of cerebral RMI. Typical symptoms of PRES include altered mental status (encephalopathy), seizure, and headache, less commonly visual disturbances or focal neurologic signs; acute hypertension is seen in > 50% cases; cerebral RMI, the key investigation for PRES diagnosis, shows cortical-subcortical, sometimes symmetrical bilateral lesions of vasogenic edema (hyper intense T2 and FLAIR signals) in cerebral areas with low vascularisation, with different patterns (classic parietal-occipital, holoemispheric, superior frontal sulcus, and partial or asymmetric); the pathophysiology of PRES remains controversial; complications like cerebral infarction or haemorrhage may determine permanent neurological abnormalities; death is possible (increased intracranial pressure with brainstem compression or cerebellar herniation). In children with malignancy PRES should be differentiated from other possible neurological complications.
Material and methods. Presentation of two consecutive cases of PRES (January, March 2015) complicating the induction treatment for ALL, with analysis of neurological manifestations, clinical and biological context of appearance, neuroimaging aspects, triggering factors, differential diagnosis,

evolution, and impact on ALL treatment.
Results. Two female patients - BTE, aged 7 years, diagnosed in December 2014 with ALL with B cell precursors, and PAM., aged 8 years, diagnosed in January 2015 with ALL with mature T cells, none with central nervous system (CNS) involvement at diagnosis, developed severe neurological manifestations (generalised polymorphic seizures rapidly followed by coma in the absence of fever) on the 27th and respectively 35th day of induction treatment (Protocol I -ALL BFM-2000 with prednisone, vincristine, daunorubicin, asparaginase, intrathecal methotrexate). Because of the critical state at the moment (severe bone marrow aplasia, coagulopathy, toxic neuropathy with constipation and cholestasis, SIADH), many different complications were suspected; with emergency biological investigations, cerebral CT scan, and multiple interdisciplinary consultations (neurology, psychiatry, ophthalmology, radiology), most of the possible causes were excluded (precedent severe metabolic abnormalities, CNS hemorrhage, thrombosis, infection, or leukemic involvement) but what caused the rapid neurologic deterioration remains unclear. The diagnosis of PRES was only established after cerebral MRI showing bilateral lesions of vasogenic edema mostly in the posterior parietal-occipital region but also in the right/left temporal and both frontal lobes, complicated with diffuse cytotoxic edema, and small parenchymal hemorrgahes. Retrospectively, a rapidly ascending blood pressure before the onset of the neurological manifestations was noted in both cases, followed by severe hypertension hardly controlled with four antihypertensive drugs at high doses (captopril, metoprolol, nifedipine, furosemid) only after 11-14 days, and resolved after one month (secondary to PRES?). Both patients had irregular fever a few hours after the onset of PRES, announcing sepsis (Klebsiella, MRSA). Emergency treatment was immediately applied (cerebral depletion, antihypertensive agents, anticonvulsant), with reversal of coma after 8 hours, and respectively 4.5 hours. The initial episode was followed in both patients by diverse neurological and psychological manifestations up to one month (myoclonus, facial and upper limb paresis, echolalia, bruxism, marked agitation, easy crying, irritability, aggressivity), and prolonged treatment with midazolam, clonazepam was needed; both are still under treatment with levetiracetam. Control MRI showed complete resolution of cerebral edema 2 and respectively 3 months after the onset of PRES, with residual mild cerebral atrophy (BTE) and minor frontal ischemic lesion (PAM). Long-term evolution was good, without neurological sequelae, and only mild psychological problems. PRES had a major impact on ALL treatment (stopped for 34/43 days) but fortunately both girls are in remission of ALL at 20/21 months after diagnosis; no relapses of PRES appeared despite other 5 months of intensive treatment for ALL (hypertension in course of protocol II was promptly controlled).
Conclusions. Induction treatment for childhood ALL associates major risk factors for PRES (hypertension secondary to corticosteroids in high doses for a long period, toxicity of chemotherapy, sepsis complicating severe bone marrow aplasia); prompt recognition and correction of hypertension are essential for the prevention of PRES in this context. Cerebral MRI is the key investigation for early diagnosis of PRES. Although the classic definition of PRES is still in use, a better name may be "potentially reversible encephalopathy syndrome" since the cerebral lesions are not exclusively posterior, neither rapidly nor always completely reversible.

Key words: posterior reversible encephalopathy syndrome, acute lymphoblastic leukemia, children

COMPLICATIONS OF CASE ACUTE LYMPHOBLASTIC LEUKEMIA Ph + AFTER ALLOGENEIC STEM CELL TRANSPLANTATION.

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Acute lymphoblastic leukemia (ALL) is a malignant disease of the bone marrow characterized by proliferation of early lymphoid precursors and replacement of the normal hematopoietic marrow cells. The allogeneic transplantation in ALL has indications in Philadelphia + / BCR-ABL + ALL and ALL with (4; 11). Allogeneic transplantation has two important roles. First: reconstitution of hematopoiesis after high-dose chemotherapy. Second: graft-versus-leukemia effect, donor cells recognize leukemia cells as non-self. We present the case of a young patient with Ph + ALL after allogeneic stem cells transplantation from a related donor, histocompatibility 100%. Because of unfavorable prognosis early relapse appear at 2 months after transplantation with >50% bone marrow infiltration with blasts. The haematological remission was obtained after reinduction + salvage treatment with clofarabine. To prevent relapse we administered donor lymphocytes infusions. The patient enters in remission and continue maintenance treatment with Imatinib 400mg / day. At 11 months after transplantation appear CNS relapse, we administered intrathecal MTX +

Dexamethasone and radiotherapy of CNS + column. Relatively favorable evolution was obtained under treatment with Imatinib. 1 year and 6 months posttransplant occure liver cytolisis signs and ascites. In ascites fluid is highlighted > 50% lymphoblasts. Leucemic skin determinations appeared too. After the administration of Cytosar followed by the infusion of donor lymphocytes febrile neutropenia and sepsis appeare leading to the death of the patient. Allogeneic stem cell transplantation has an absolute indication in ALL with BCR-Abl mutations / t(9.22) Ph+ but this disease has a negative prognostic factor, with early relapse and resistance to treatment.

INTRAMURAL HEMATOMA AND SMALL INTESTINAL OCCLUSION IN A PATIENT WITH SEVERE HAEMOPHILIA A - CASE REPORT: PROPHYLAXIS - COST / BENEFIT?

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Haemophilia A is a rare bleeding disorder (~1:5000-10.000 males), most often inherited (X-linked recessive disease), characterized by factor VIII deficiency. The optimal management of the haemophilia patients is complex and extremely costly, requiring the use of replacement therapy with coagulation factor concentrates during the entire life span as well as the treatment of chronic and acute complications.

Intramural haematoma of the intestine is a very rare complication of this disease. According to the literature, there are 33 described cases of haemophilia patients with intramural hematoma of the gastrointestinal tract from 1964 to this day. Some of the main causes are trauma, intestinal pathological conditions and the widespread use of nonsteroidal anti-inflammatory drugs (NSAIDs) in the treatment of chronic arthropathy.

FAMILIAL AMYLOIDOSIS POLYNEUROPATHY TRANSTHYRETIN TYPE VARIANT GLU54GLN.

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Transthytertin familial amyloid polyneuropathy (TTR-FAP) is characterized by extracellular deposition of abnormal fibrils derived from misfolded, but normally soluble transthyretin (TTR) molecules. The disease is caused by point mutation within the TTR gene that is inherited in an autosomal dominant fashion. There have been identified over 100 such mutations that lead to destabilization of the physiological TTR tetramer. As a result, many of the monomers have a tendency of spontaneous conformational changes and self–aggregation.

Initially, it predominantly affects small unmyelinated nerve fibers and results in dissociated sensory loss (loss of sensation for pain and temperature). Autonomic neuropathy typically accompanies the sensory deficits in the early stages of the disease (orthostatic hypotension, constipation alternating with diarrhea, erectile dysfunction, anhydrosis and urinary retention or incontinence).

Later, the motor fibers are involved and cause rapidly progressive weakness and gait disturbances and finally the patient becomes confined to bed.

We present the case of a 51 year old male patient, that had a sister who died at the age of 49 from a cardiac disease and his mother died at the age of 50. The onset of his disease was in 2012 with diarrhea of unknown cause (rectum biopsy – Congo Red negative). Afterwards, in 2014, he presented paresthesias and muscle weakness in the lower limbs. In March 2016 he was admitted to the Neurology Clinic (Fundeni Clinical Institute), and the EMG established the diagnosis of Sensorimotor axonal polyneuropathy. The patient was then admitted to the Hematology Clinic, with extreme fatigue, peripheral edema, painful lower limb paresthesias that progressed to knee-level, orthostatic hypotension, bowel disorders and cachexia. Investigations were performed for the diagnosis of amyloidosis (familial or primary) and it was established to be Familial amyloidosis transthyretin type (Glu54Gln) with systemic involvement: Cardiac (restrictive cardiomyopathy, paroxysmal atrial fibrillation), Nervous system (Sensorimotor axonal polyneuropathy stage I subtype II), autonomic nervous system (orthostatic hypotension, chronic diarrhea)

The patient received cardiac and neurological treatment and he was periodically evaluated for polyneuropathy and cardiac impairment, which were stable 4 months after the diagnosis, but the orthostatic hypotension was worse.

We are currently taking steps for the initiation of Tafimidis treatment (transthyretine stabilizer) with the intent of reducing the amyloid deposition and preventing the evolution of the disease.

Familial amyloidosis transthyretine type is an incurable disease, with a median survival of 7-10 years after the onset of symptoms. Liver transplantation is the standard therapy for eligible patients because it stops the synthesis of the mutant TTR. Tafimidis and other transthyretin stabilizers are new agents, still under investigation.

MULTIPLE MYELOMA-PRIMARY CHEMORESISTANCE - TUMOR DEVELOPMENT WITH EXTRAMEDULLARY PLASMACYTOMAS: CLONAL PROGRESSION OR CLONE CHANGE?

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In this era of new innovative drugs, myeloma remains a difficult to treat hematologic malignancy. This trait is due to resistent phenotypes both at diagnosis and developing a resistent form during the course of the disease. Actual mechanisms underlying drug resistance in multiple myeloma are not fully understood. In this article, we describe the case of a 67 year old patient with multiple cardiac pathology associated that addresses the clinic in October 2014 for asthenia, fatigue, palor. The patient presented with suspicion of megaloblastic anemia, but increased plasma infiltrate in bone marrow aspirate led investigations to the diagnosis of Multiple Myeloma IgG kappa std IIIA, multiple lytic lesions, chronic kidney disease std III. The patient initially received chemotherapy with cyclophosphamide and dexamethasone, which was associated with Velcade after receiving bortezomib's approval. Given the fact that the patient had no indication of autologous stem cell transplant and showed progression of bone lesions during chemotherapy, it was decided to change the protocol type to VMP protocol. Due to minimal response to treatment, we changed again the protocol to Thal-Dex . The tests we have done to evaluate the disease response to treatment highlighted the lack of response to therapy and thorax, abdomen and pelvis scan performed due to repeated rectal bleeding detected multiple osteolytic lesions and the occurrence of multiple tumors, imprecisely demarcated, located in the abdominal cavity with pelvic extension to the left. It was considered – primary refractory disease- to all lines of therapy (were administered proteasome inhibitors, iMIDs, melphalan, cyclophosphamide, corticosteroids) with rapid progression under therapy, reason why in agreement with his family, we opted for palliative treatment, the patient died in 18months after diagnosis.

THERAPEUTIC RESPONSE AFTER AUTOLOGOUS STEM CELLS TRANSPLANT: ROLE OF FREE LIGHT CHAINS ANALYSIS.

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Intact monoclonal immunoglobulins or fragments synthesized in plasma cells from a malignant proliferation of B lymphocytes is a good indicator that could provide better insight in evaluating the response and disease progression in patients with multiple myeloma.

The aim of this study is to analyze the role and efficiency of free light chains analysis in monitoring patients with multiple myeloma treated by high dose therapy and after autologous stem cell transplantation (ACT).

For diagnosing and monitoring of multiple myeloma we used four methods: FLC assay, serum protein electrophoresis (SEP), serum immunofixation (IF) and serum immunoglobulin quantification. The FLC assay (FREELITETM; Binding Site) and serum immunoglobulin quantification were performed on a Dade Behring, BN ProSpec automated nephelometer and SEP and IFE were performed on a SEBIA electrophoresis automated analyzer.

During this study we analyzed samples coming from patiens with IIMM (intact immunoglobulin multiple myeloma), LCMM (light chain multiple myeloma) and renal amyloidosis.

For all those patients with IIMM we determined the grade of correlation between FLC (free κ, free λ and κ/λ

ratio) and two other markers: M-protein and total intact immunoglobulin, at diagnosis and during the treatment.

For statistical evaluation we used two correlation coefficients: Spearman and Pearson calculated with the SPSS (Statistical Package for the Social Sciences) program.

FLC assay provide important markers for diagnosing and monitoring patients with LCMM and renal amyloidosis, in these diseases electrophoresis failing to provide an answer. Due to their shorter half-lives compared with immunoglobulins, free light chains allow a more sensitive measure of monoclonal protein production.

Keywords: multiple myeloma, free light chains (FLC), autologous stem cell transplant.

THE IMPACT OF MOLECULAR RESPONSE ON OVERALL SURVIVAL IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA TREATED WITH TYROSINE KINASE INHIBITORS: TEN YEARS OF EXPERIENCE IN A SINGLE CENTER.

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During 2004-2013, 189 CML patients were diagnosed and monitored in Hematology and Bone Marrow Transplant Department of Fundeni Clinical Institute, Bucharest and the impact of molecular response obtained with TKI on overall survival was observed. A slight male predominance was noticed and the median age at diagnosis was 50 years. From all prognostic scores at diagnosis, EUTOS had most impact on overall survival, followed by Sokal and Hasford score. At diagnosis, 87,8% were in CP, 7,4% in AP and 4,8% in BP. Medium survival time for CP was 85 months, AP was 77 months and BP was 4,66 months. The most used TKI in first line was Imatinib but 55 patients needed second line and 15 patients needed third line TKI due to failure according to ELN 2013 recommendations. The most frequent p210 BCR-ABL1 transcript type was b3a2 followed by b2a2 and b3a2 + b2a2. The achievement of MMR at 18 months was associated with improved overall survival. In the first 60 months, all events (deaths) were produced and were associated with high transcript levels (>10%) at 6 months monitoring time. The median survival was according to the type of molecular response. At analysis, 82,96% of patients were alive and 17,03% were deceased.

This work was supported by the grant PN 41-087 from the Romanian Ministry of Research and Technology. The authors express their gratitude to European LeukemiaNet for their permanent support.

Key- words: CML= chronic myeloid leukemia, CP= chronic phase, AP= accelerated phase, BP= blast phase, TKI= tyrosine kinase inhibitors, MMR= major molecular response

TP53 SEQUENCING IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA BY SANGER & NANOPORE SEQUENCING.

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Introduction. Chronic lymphocytic leukemia is the most frequent leukemia in adults, in most cases being an indolent disorder. Nevertheless, the European Research Initiative on CLL (ERIC) recommendations include the identification of TP53 mutation by sequencing to define a subgroup of patients with poor response and survival to standard of care [Leukemia 26:1458, 2012]. This poster describes the implementation process of the molecular diagnosis by Sanger sequencing in the UEHB molecular pathology laboratory, and a comparison with a 3rd generation sequencing using the MinION system (Nanopore).

Materials and Methods. The protocol used for Sanger sequencing is the one recommended by ERIC and adaapted for the existing sequencing system (GeXP, Beckman Coulter). In summary, DNA is extracted, exons 2-9 and 11 (which require the same conditions) are amplified with the IARC recommended primers, PCR products are purified using the QIAquick PCR Purification kit (Qiagen), followed by sequencing amplification (GenomeLab DTCS Kit, Beckman-Coulter), PCR products purification by ethanol precipitation and microcapillary analyses. Results are interpreted by comparison with the IARC TP53 database. For the Nanopore sequencing analyses, the same purified amplification products are used as per the producer's recommendation (Genomic DNA Sequencing Kit SQK-MAP): the amplicons are subjected to an end-repair process (NEBNext End-Repair Module, New England Biolabs), then purified

with AMPure XP (Beckman-Coulter) and free-ends are integrated with NEBNext dA-tailing module (New England Biolabs). This is followed by the ligation of the adapters provided in the Nanopore kit and separation of the products by magnetic microbeads, after which the library is sequenced in a MinION cell for 48h. Results are aquisitioned using the MinKNOW program, base identification is made through the Metrichor on-line program. Sequences alingment si mutation identification is made by the BLASR and samtools mpileup.
Results. The results of Sanger sequencing and their comparison with the sequences obtained using Nanopore technology are presented.
Conclusions. The Sanger analyses protocol of TP53 mutation status in CLL patients can be implemented and is one the most efficient from the cost/benefit ration aspect. Although it has a high error rate, Nanopore sequencing could be useful for such a diagnosis process using advanced analyses software solutions, and it also presents the added benefits of portability and a lower price vs. 2nd generation sequencing methods.

ADAPTING IBRUTINIB TREATMENT FOR A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKEMIA STAGE IV RAI – CASE REPORT.

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Introduction. Chronic lymphocytic leukemia (CLL) is the most frequent leukemia in adults, with a mean diagnosis age of 65 years. It is most often an indolent disorder which doesn't require treatment. The current standard of care for patients with good performance status is immunochemotherapy – R-FC. Up until recently therapeutic options for patients with multiple comorbidities, ECOG score 3-4, or treatment refractory cases were limited. The introduction of ibrutinib, Bruton's tyrosine kinase inhibitor, as a therapeutic option for refractory cases, including patients with 17p deletion and/or TP53 mutation offers new perspectives for these subgroups of patients. In thus poster we present the case of a patient cu CLL stage IV Rai, unresponsive to alemtuzumab and the tailoring of ibrutinib treatment.
Case Report. A female patient initially diagnosed in 2009 at 64 years of age after a routine CBC evaluation with stage II Rai CLL. Initial CBC: WBC= 23 700/μL, w. 72% lymphocytes, Hgb= 13.5 g/dL, PLT= 223 000/μL, with smudge cells after peripheral blood smear examination, with a high LDH value =406 U/L. Immunophenotyping revealed 77% lymphocytes, of which 70% B lymphocytes CD19+, CD5+, CD20+, CD43+, CD79b-, CD23+. The patient was monitored until 2014 when she was admitted for significant B signs. The patient was diagnosed with CLL stage III Rai, the CBC revealing WBC= 307 000/μL, w. 70% lymphocytes, Hgb= 11.2 g/dL, PLT= 172 000/μL. Due in part to the patient's age at the time (69 y.o.) we opted to start treatment with alemtuzumab. Between May 2015 – December 2015 the patient underwent immunotherapy receiving a total dose of 173 mg of alemtuzumab. In December 2015 the patients was diagnosed with progressive disease – stage IV rai CLL, WBC= 72 000/μL, 93% lymphocytes, Hgb= 7.4 g/dl, PLT= 6 000/μL. Taking into account the patient's age and the lack of response to alemtuzumab we opted to start treatment with ibrutinib. Because the patient presented severe thrombocytopenia and also had a history of spontaneous epistaxis and hemoptysis, to limit the risk of a major hemorrhagic event ibrutinib treatment was started with 140 mg/day (1 capsule). One month after treatment initiation the CBC showed: WBC= 72 800/μL, Hgb= 9.1 g/dL, PLT= 50 000//μL. After 4 months of treatment the were no adverse events with a therapeutic conversion to stage III Rai CLL – WBC= 17 000/μL, Hgb= 9 g/dL, PLT= 123 000/μL.
Conclusions. We presented a case of stage IV Rai CLL refractory to 1 line of treatment which had a very good response to reduced-dose ibrutinib treatment. This case reflects the need to perform a careful evaluation each patient and to tailor the treatment in order to obtain the best possible results taking into account the benefits/risks ratio.

ROMANIAN CHRONIC LYMPHOCYTIC LEUKEMIA PILOT REGISTRY - CHRONIC LYMPHOPROLIFERATIVE DISORDERS SCREENING PANEL IMPLEMENTATION.

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Background. Chronic lymphocytic leukemia (CLL) is the most common chronic lympho-proliferative disease with an incidence estimated at 4: 100 000 / year, with an increase in incidence over the age of 80 on 30: 100 000 / year. The etiology of this condition is not known, but they were described multiple risk factors and infectious factors or family history. It is a heterogeneous disorder whose pathogenic mechanism is assumed to be the result of interaction between environmental factors and host factors as cases are divided into several categories depending on prognostic genetic changes present. This heterogeneity highlights the need for a national registry to track these patients to better stratify them for analysis and discovery of new prognostic factors and the development of national management of these patients, with the objective of subsequently enable an easier implementation the concept of personalized medicine for patients with this disease in Romania.

Aim. The present study proposes the introduction of a screening panel by immunophenotyping in patients with suspected LLC lymphocytosis and to assess the actual incidence of CLL in Romania on a constant panel.

Material and method. Peripheral blood samples were collected on EDTA whole from patients with clinical suspicion of LLC / chronic lymphoproliferative syndrome. For diagnostic immunophenotypic was used for screening a panel consisting of monoclonal antibodies: CD19, CD20, CD5, CD23, CD43, CD79b. For creating this pilot registry data were recorded placed on the sex, age, total leukocyte count and diagnosis.

Results. Of the 840 evaluated 450 samples (53.6%) of cases were diagnosed with CLL. A total of 72 cases were diagnosed with monoclonal B lymphocytosis / small lymphocytic lymphoma. The average age of patients diagnosed with CLL was 66.9 ± 10.57 years, with median age of 67 years, from the age of 75 years were registered 116 patients diagnosed with CLL; the ratio B / F was 1.6; the average number of leukocytes was 62 ± 74 113.9 008.9 WBC / ml, and the maximum was 527 010 leukocytes / ml. They were diagnosed 105 (12.5%) cases of malignant non-Hodgkin's lymphoma (NHL) marginal zone, and 35 (4.1%) cases of mantle cell lymphoma (MCL). Of the 840 patients 132 (15.71%) showed no detectable changes by flow cytometry.

Conclusions. This is the first study using the same protocols to diagnose cases of CLL in several centers from different regions. The report positive diagnosis about 85% is considered very good, and supports the diagnostic ability of this model to identify new cases of chronic lymphoproliferative in Romania. These preliminary data are very useful to assess the true incidence and etiological factors of occurrence LLC in Romania. This is the premise for the creation of a biobank for CLL program that provides the opportunity to study the characteristics of patients with CLL in Romania.

SECTION TRANSFUSION MEDICINE
SCIENTIFIC SESSION

HAEMOVIGILENCE.

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BTS Constanţa

Transfusion treatment is saving lifes, but it still involves partially controlled risks. Professionals and practicioners should be awared of these risks, to foresee and reduce them by using the available solutions/methods, for a reduced negative impact on patients/donors.
Root-cause analysis of adverse reactions and untoward events is essential to identify un-foreseable risks, aditional preventive and/or corrective measures to avoid risks and finally improve transfusion safety. Succesfull analysis of transfusion effects on patients, as well as of blood donation on donors is relying on a consolidated data-base of adverse reactions and events with variable impact on blood safety.

Haemovigilance is the 'systematic surveillance of adverse reactions and adverse events related to transfusion' , including their registration, reporting and analysis, with the aim of improving transfusion safety. The added value of a functional haemovigilence system is conditioned by the correct understanding of its goal, as well as by a common, unitary approach by all professionals involved. Lack of of clarity on roles and responsibilities of personnel involved, lack of a national coordinating structure to elaborate guidelines, a common set of definitions and procedures, as well as insufficient knowledge regarding haemovigilence are all negatively impacting factors on the functionallity of the Romanian haemovigilence system.

The educational session is meant to introduce to the participants, in a logical, informative and instructive manner, the main aspects defining a haemovigilence system.

The regulatory frame for implementing a haemovigilence system, EC/DG SANCO guide for a common understanding to report the severe adverse reactions and events, internationally adopted clasifications and definitions are presented to the participants. Aditionally, real cases are described.

The organisers hope that topics included will bring clarifications to several expressed issues with regards to practical implementing aspects, becoming the starting point for an increase in the reporting rate of adverse reactions and events in blood establishments and hospitals.

INCIDENTS AND ACCIDENTS RELATED TO BLOOD DONATION.

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* CTS Hunedoara, **CTS Deva,

Haemovigilance is defined as a set of procedures for monitoring the incidents and serious or unpredictable reactions occurred both the donor and the receiver also epidemideologica donors and surveillance (Directive 2002/98 / EC of the European Union regarding the blood).

Romania, as a EU member country, organized legislative haemovigilance specific legislation transposing Directive EC in Romanian (Order MS.1228 / October 2006).

Haemovigilance is to guarantee the quality and safety of labile blood products and their safety administration.

Donations they provided reactions and serious incidents that have influenced the quality and safety of blood must be recorded and analyzed. The result of this must be measures taken to hospitals and CTS sites to prevent these reactions and incidents and to ensure the safety of blood transfusion.
Generic types of accidents- Genera, Local
Side effects - severe, non-severe
Imputability level: Safe perhaps Possible uncertain excluded.
Deva-Hunedoara CTS level I did a review of serious incidents related to the act of donation.

INTERNAL QUALITY CONTROL IN VIROLOGY.

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* CTS Deva, ** CTS Hunedoara

Internal quality control (CIQ) laboratory offers clear, quick, easy to understand, decisions based on results which were validated.

The specifities of internal daily control are (CIQ): these control samples are performed in the same conditions as series work samples; the results of these internal controls must be guaranteed and known; Laboratory Officer has the duty to: organize the daily internal control, use the correct information given by CIQ, correct anomalies indicated by CIQ, inform responsibility for quality control and observations related to CIQ, apply corrective action in case of non-validation of CIQ.

Laboratory Officer responsible for: functioning equipment, validation of reagents; validation of immunohematological investigation; traceability in immunohematology laboratories; internal evaluation of immunohematology laboratories.

To remove all sources of error, reflected on the results, internal quality control monitors the course, all laboratory activities, along preanalytical phase, analytical and postanalitical phase.

Internal quality control preanalytical phase requires knowledge of all sources of error and their elimination results (70% of error sources lab results come from preanalytical phase).

Internal quality control in analytical phase begins with choosing suitable working method as: specificity, accuracy, detection limit, interval and ratio analytical efficiency / cost. Once established the method, each laboratory must verify the reference range and to establish its own reference range, depending on demographic variables, geographical or socio-economic ones.

The used Kontrol sera (blood control) must check materials with certified quality, which have predetermined values of the analytes with boundaries that define the expected change, have normal and pathological concentration level and good stability over time.

Internal quality control postanalytical phase involves: Validation by the laboratory which is responsible for; Dissemination of results expressing the results obtained from the analysis, clear, precise, unambiguous and in relation to the reference ranges. The issued analysis report is validated by the signature of the executor and head of the laboratory; Storing samples; Eliminating samples

Performance analysis using quality controls is retrospective, but has great utility for: The ensurance of good traceability to international measurement units; Identification and remediation of the issues related to human activity or equipment; Education and training of the staff; Market research reagents and equipment; Obtaining more trust and customer confidence in the competence of the laboratory.

Conclusion: Internal quality control - is indispensable to detect errors and must apply immediate corrective measures.

THE IMPORTANCE OF BACTERIOLOGICAL BLOOD CONTROL IN ORDER TO INSURE A QUALITY BLOOD PRODUCT TO THE HOSPITAL SUPPLIERS.

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BTS Braşov

Introduction: Through the methodological letter initiated by the department of Controll/Quality Hematology and Bacteriology, begining with the year of 2014, the quality controll of the blood and its components unit is to be made strictly by following the steps stipulated in the COE methodoligy and norms of the Preparation, Use and Quality Assurance of the blood products Guide coordonated with the national laws into force at the present time. (ORD.Ms.1237/10.07.2007, inforced and completed by lows: 13361/19.05.2011 and 814/14.08.2012).

The quality control consists in an accurate evaluation of the microscopic aspect, the completed check up of the bacteriological, haematological and biochemical control. The purpose of the bacteriological control is to continously monitorisation of the bacterian contamination risk of BC.

Case showing: The submitted evaluation is from 2015, when 312 bacteriological tests have been taken as the BC.

Results: Of those reviews only 7 blood components were proved to being positive at the end of the incubation period –the distructive method- in the automatic BACTALERT system the ratio is of 0.22 percent.

Conclusions: The specified ratio must not pass the limit of 0.2 percent of the tested samples used in the bacteriological control. In the case that the value of the specific contamination ratio is higher than 0.2 percent the overall review of the procedures for collecting and processing are required.

The bacteriological controll of BC is final purpose to determine the decrease of the bacterian contamination through the approval of definitive and firm measures that can guarentee a safer transfusional process.

IGNORING THE PRE-TRANSFUSION TESTING STAGES , RELIABLE SOURCE OF HEMOLYTIC TRANSFUSION ACCIDENTS.

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The incompatible transfusions in the erythrocytes' systems, have as result hemolytic reactions intra or extravascular or aloimmunisations anti-erythrocytes, threatening patient's life and / or his transfusion future.

To ensure the security of erythrocyte transfusion, in a as much as possible ideal close ratio, there are mandatory set of rules and steps, which must be followed by the staff of the units, which do the transfusion therapy. The responsability of following accurately these steps is in the doctors' hands, of the blood transfusion unit (BTU) , doctors who treat them and especially in the hands of the

respective nurses of the units, the point where the transfusion is done.

The first step, very important, is to ensure correct identities of the blood sample collected from the patient, registering in the moment of collected time and in front of the patient notifying the data on the test tubes with the blood collected in. Later, at the BTU, will be the submission of the received samples, determining the right 0AB group and D (the rule of "two"), researching the irregular anti-erythrocytes antibodies, doing the major tests of compatibility with the request blood units received, filling the compatibility paperworks , which will go with the compatible unit.

At the place where the transfusion is done, the transfusion staff will check the layout and the data's blood unit, which was received, to be same with the patient's data and coresponding to the unit, and checking in the end everything near the patient's bed ("bedside") the 0AB/ D group and the donor's, on the specific corresponding card. This last checking/ verification of the group is the last chance to avoid any incompatible transfusion in the 0AB system, supposing that not all the steps were done correctly before.

After following all these steps, the transfusion act must be monitored on its entire period of time, taking notes in the transfusion data sheet, at well-defined time intervals of the key vital signs.

THE ULTIMATE PRE-TRANSFUSION CONTROL AT THE PATIENT'S BED – ESSENTIAL ROLE IN PROVIDING THE TRANSFUSION QUALITY AND SECURITY (CASES REPORT).

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The Blood Transfusion Center of Braşov

Introduction: By its issues, blood transfusion involves multiple risks, one of the major residual risks being the immunologic incompatibility between the donor and the recipient.
All the prior stages of the transfusion are important and they are part of a work algorithm thus conceived to ensure transfusion security. Despite all these, the ultimate control at the patient's bed is most of the times, the same as in the cases we analyzed, the most important.

Cases: We analyze two hemolytic accidents occurred by OAB incompatibility and case where the identity of the patient from which pre-transfusion samples were taken was not checked.

Conclusions: The studied cases showed that the ultimate pre-transfusion control at the patient's bed was not made, there is no standard operating procedure and if there is such a procedure, it was not applied.

The ultimate control at the patient's bed did not represent a strict rule that must have been respected by the practitioners. The ultimate pre-transfusion control at the patient's bed is absolutely essential to avoid the consequences of potential OAB / Rh (D) grouping errors, errors of identifying the recipient or errors in administering the transfusion unit.

The ultimate pre-transfusion control at the patient's bed is the last chance to prevent a serious hemolytic transfusion accident or even death and to ensure a high degree of transfusion security.

TRANSFUSION MEDICINE SECTION
ORAL PRESENTATIONS

DONOFORIA - PSYCHOLOGICAL FACTORS INVOLVED IN BLOOD DONATION; PRELIMINARY RESULTS.

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Background: The actual need of blood products reported by the Romanian hospital system is rarely met by the blood collection centres, mainly due to challenges associated with creating and maintaining a stable poll of blood donors. In order to adequately address this challenge, a better understanding of the barriers and motivators of blood donation behaviour is needed. In our study, we are using the Theory of Planned Behaviour (TPB) to analyse the attitudes towards the behaviour as well as the facilitating factors for blood donation. Other types of evidence based antecedents were also considered.

Material and methods: A 29 item survey was developed and widely disseminated in the general population via social media networks and emails, which has resulted in a total opportunistic sample of 1322 completed questionnaires. The survey was developed on the basis of previous work conducted by Godin and co. (2005) and by Bednall & Bove (2011) and included factors such as: the anticipated regret, the perception of control, the attitude toward blood donation, self-efficacy, moral norm, social norm, fear of donation, prosocial motivation, convenience of collection site, the reputation of the donation agency, the perceived norm for donation, the incentives, the satisfaction with the staff and the service.

Results: Respondents were predominantly women (64.4%), from an urban setting (82,1%), having completed a bachelor or master degree (64.4%), employed (70%) and with a mean age of 32,72 (SD=7,97). Among these, 69,1% have never donated blood, 20,8% are single time donators and only 10,1% are repeated donors. The strongest facilitators identified were related to prosocial motivation and the most important deterrents were connected to the satisfaction with staff and service, followed by lack of awareness, not being asked to donate and lack of time.

Conclusion: These preliminary results indicate that, despite repeated campaigns conducted to increase the blood donation, the level of awareness is still low in the general population. Also, based on our results, we recommend that future campaigns should address more directly the prosocial motivation and should also aim to increase the trust in staff and blood donation services.

THE IMPACT OF A STRONG MOTIVATION FOR BLOOD DONATION ON THE FREQUENCY OF ADVERSE REACTION IN DONORS.

F. Neagu, C. Posea, C. I. Nedelcu, E. C. Golgot
BTS Bucureşti

During a rock concert in Bucharest, a fire broke out and there where many injured and dead.

The event was covered live by all the media outlets, thus generating a lot of emotions among the population. This happened primarily because the victims were mostly young people, having a good time. Whit the desire to help as efficiently and as fast as possible with the starting of the election treatment common in such cases, the people who found out about the disaster realized or where informed to start by donating blood. As such, during the night of 31 of October 2015, the main challenge that the Bucharest Blood Transfusion Center faced was to manage the sudden influx of highly motivated individuals, that wanted to help by donating blood. It was the first time in Romania when the blood collection happened at night. In the following days the number of potential donors doubled. Many studies associated factors like young age, first time donor status, high waiting time (4 to 8 hours), with higher adverse reactions (AR) among donors.

Although all of these factors, and more, cumulated in the time period following the disaster, the AR frequency did not increase.

One explanation could be that the collective emotion and the altruistic desire to save lives, generated a very strong motivation. This led to a decrease in unwanted reactions in donors.

HAEMATOLOGICAL PARAMETERS TO THE CTS DONORS, PERIOD 01.06.2014-01.06.2016 IN ARAD.

L. Păcurariu, L. Ardeoan
CTS Arad

In this study, we considered the important hematological parameters for the security of blood donors and also for the quality of the blood components

obtained, as well as the therapeutic efficiency of the blood products to the transfused patients. Track parameters are: number of white blood cells, hemoglobin and platelet counts.

Results. Total of 1,048 temporary exclusions from donating based on low hemoglobin below the allowable donation, from a total of 10321 potential donors, presented in this period. Among them were 750 women and 298 men; respectively 281 women from rural area and 469 from urban area; men were 98 from rural area and 199 from urban areas.

Were excluded from donation 10.15% of donors, based on hemoglobin below standard. Leukocytes: 71 donors were excluded from donation based on increased leukocyte 11,000 / mm3 out of 10321 potential donors, present in this period. Thrombocytes: in this period, was performed completed heleucograma to a total number of 15 421 donated units. It stated a total of 618 units of platelets <150,000 / mm3 (ie 4%).

Conclusion: The rather large number of donors with changed hematological parameters out from the admissible limits, requires searching and solving the causes that led to these changes, for the donor loyalty, reduction of losses and cost efficiencies.

THE IMPORTANCE OF COMPLETE BLOOD COUNT (CBC) WITH DIFFERENTIAL BLOOD COUNT AND THE IMPORTANCE OF RX PULMONARY RADIOSCOPY PERFORMED BEFORE BLOOD DONATION.

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Floreasca Emergency Clinical Hospital, Bucharest

Beckground: The exclusion of blood donors presenting risks is a vital step for transfusion safety, as well as in what donors' eligibility is concerned. This is currently done through the process of anamnesis, by completing the pre-established written form, through medical consultation and, also, with the help of complete blood count and of serological tests (which identify the presence of different dieases such as syphilis, hepatic viruses B and C, HTLV and HIV). Donors who are considered to be eligible for donation following a medical examination are subjected to pre-donation biological tests, aiming at ensuring both their protection, and the quality of blood products made of the donated blood. The hemoglobin level of potential donors is usually determined by testing peripheral blood with a non-invasive device, namely a HaemoCue 201 portable hemoglobinometer which mesures only the level of hemoglobin.

Methods: In UTS Floreasca, hemoglobin was tested for all the donors who had been considered eligible for donation. With the help of an automatic analyzer-Sysmax XT 4000-, which is able to test the complete blood count with 5 differentiations, thus obtaining details regarding the number of leukocytes, eosinophils, lymphocytes, basophils and platelets. Although Rx pulmonary radioscopy is no longer compulsory (and in what regards blood collected during mobile blood donation units, this is impossible to test), we have come to the conclusion that this is an important eligibility criteria, because of the deterioration of the standard of living, of population health and taking into account the current socio-economic context.

Cases: We have done a statistical study, spanning 4 years, during 2012-31st June, 2016, on a number of 22257 possible blood donors within UTS Floreasca, regarding the importance of the complete blood count with 5 differentiations and of the Rx pulmonary radioscopy in eliminating the potential donors who presented modifications of the differential blood count and/or in eliminating donors who presented modifications of the chest-pulmonary image. Voluntary blood donors came to our hospital in order to donate blood due to humanitarian reasons or to help a relative or a friend hospitalized here. Also, many voluntary blood donors who were interested in payment (a possible income for living, namely vouchers given after donation) for their blood donation came.

Results: 9217 potential donors were rejected after the anamnesis, the medical examination and after the pre-donation biological tests, 329 were rejected after testing their complete blood count, 78 were rejected from blood donation because of their chest-pulmonary image.

6369 complete blood counts were taken, out of which 184 presented high leukocytes and 130 had high eosinophils, so these persons were not accepted as blood donors. 6118 Rx pulomnary radioscopies were performed, out of which 64 presented alterations with TBC aspect in an acute phase and having TBC sequelaes, and 14 presented other modifications that made blood donation impossible for them (viral, malignant tumors, asthma).

Thus, taking into consideration the low number of blood donors found with a pulmonary patology (active TBC, TBC sequelaes), the haematological modifications (leukocytosis, thrombocytopenia, eosinophilia), as well as the level of costs for tests, we would like to propose a debate in which to decide whether to continue or not to do these types of analyses. I would like to ask you: would you accept, in case of necessity, contaminated blood?

Conclusions: The rejection of a blood donor from donating after the anamnesis, the medical examination and the pre-donation biological tests, underline the importance and efficacity of these tests in ensuring the quality of the tranfusion process.

THE EFFECT OF PLATELET CONCENTRATE BY APHERESYS COLLECTION WITH MCS + HAEMONETICS BLOOD CELL SEPARATOR AFTER 5 REPEATED DONATIONS.

E.Negoiță
BTC Bucharest

Introduction: The present study analyses the modifications in platelet count, in hematocrit and platelet concentrate colected using MCS + Haemonetics blood cell separator after 5 apheresys donations.
Aim: Knowledge of haematological changes which appear after repeated donation by apheresys and the changes in the colected platelet concentrate could influence the legal time lapse between donation sessions and the selection of donors.

Material and method: The study group consisted in 100 donors with repeated platelet donation by apheresys using MCS + blood cell separator.
Results: After 5 consecutive donations at 30 days interim, decrease in platelet count was registered on 25% of the donors in the study group, decrease in haematocrit appeared on 49% of the donors and decrease in platelet concentration in the platelet concetrate was found on 12% of the donors.
Mean platelet concentration was 3,24 x 10 11 on the first donation and 4,15 x 10 11 after 5 consecutive donations for the donors in the study group.

Conclusions: Multiple consecutive platelet donations by apheresys using MCS + Haemonetics blood cell separator does not produce significant decrease neither of platelet count or in hematocrit on the donors nor the platelet concentration in the platelet concetrate.

FLOWCYTOMETRY EVALUATION OF SURFACE ANTIGENS IN PLATELET PRODUCTS.

I. Dumitru, A. Alexe, H. Bumbea
Transfusion Department, Emergency University Hospital Bucharest

Introduction: Flow cytometry allows the analysis of multiple antigens on the cell surface. At the moment there are multiple protocols for detection of various platelet abnormalities like Glanzmann Thrombasthenia, storage pool disease, diminished activity in patients treated with antiagregants. In this regard we will try to implement such a protocol as an method of testing platelet products quality and the possibility of using it for assessment of degrading platelet function with the approaching expiry of the product

Materials and metods: Our experiment aims to create an simple and specific protocol for detection of surface platelet antigens from the test columns of platelets products using a classic diagnostic protocol. In this regard we use a panel with CD41, CD 61, CD42, CD42b to which we added CD62p (to assess platelet activation) and CD3, CD19 to detect lymphocytes.
Results: In the study group we observed an slight modification of the expression of antibodies associated with storage granules (CD42a, CD42b) and we determinated the posible leucocyte contamination (CD3, CD19).

ORTHO VISION – A NEXT GENERATION EQUIPAMENT DESIGNET TO HELP IN IMUNOHEMATOLOGIE LABORATORIES (COMPARATIVE STUDY).

A. Zagrean
C.T.S.M.B

Objective: The aim of this study was to monitor and to compare various automatic in the CTSMB endowment for a period of 4 months.
Material/method: Equipments: the OrthoVision analyzer (Ortho), fully automated system Qwalys (Diagast), semiautomatic Ortho BoiVue System (Ortho) The number of 5640 samples were taken and processed for ABO / Rh / phenotype / DAI tested routinely with microplates and cassettes . Both systems Ortho use the same Ortho BioVue column agglutination of glass beads contained in a cassette , differing only technology used . If semiautomatic System reading and interpretation of results was done by a technician, Automatic Ortho Vision patented imaging system delivers results at a high resolution and if they were made automatically and have an internet connection to the CTS informatics program.

Samples were monitored by using informatics system and archives data study.

Results: 128 samples (2,27 %) DAI pozitiv : 66 Neutral, 21 Mixte and 41 samples AHG poly; only 3 cases isn't identified on Ortho Vision : 2 Anti Cw and 1 Anti M (Neutral); 65 samples (1,15 %) were D weak and D partial from different category, tested by Coombs; 7 cases isn't identified on Ortho Vision; 50 samples were testate for compatibilities.

Conclusion: The automatically Ortho Vision system is especially good for CTS with a low number of donors. The benefits are precision and accuracy giving the ability to monitor every step in the process and created a real time interaction to review resultants. Reduces manual interaction and minimizes the potential for error. The fact that it can connect to the computer system

simplifies data transmission and ensure their safety

DAY MATE – AN INOVATIVE AND FULLY AUTOMATED SYSTEM FOR IMUNOHEMATOLOGIE (EVALUATION).

A. Zagrean
Lab.Imunohematologie C.T.S.M.Bucarest Roumania

Objective: The aim of this study was to evaluate and validate the new automated method DAYMATE S from DAYmedical SA (for a period of 2 months) by comparison to the standard automated method in use .
Material/method: Equipments: fully automated DAY MATE S (DAY medical) Qwalys 3 analyzer (Diagast), semiautomatic system DiaMed (DiaMed)

The DAYmate S is a fully automated system that uses a new concept, having the reaction support represented by a planar disc with an innovative shape , in which is distributed automatically gels and reagents depending on configuration and selection of required tests , thus providing maximum flexibility in imunohematological testing.

The number of 1000 samples were taken and processed for ABO / Rh / phenotype / DAI (including 50 compatibility test) tested routinely with cassettes .
Both systems DAYMATE and DiaMed use the same column agglutination in gel,
Both systems DAYMATE S and Qwalys 3 are fully automated analyzer
Samples were monitored by using informatics system and archives data study.

Resultates : AB0 blood group distribution of the samples: 44.5% A ,40.3% O,11.3% B and 3.9% AB; for AB0 forward and reverse grouping DAYmate provided a correct resulting 96 % of the samples (38 were not interpretable : NI); for Rh (-): 21 of the 950 donors were known as weak or partial D. DAYmate tested 10 of them positive, 1 as negative and 10 as NI or possibly weak D; the antibody screening performance was 99.4% for DAYmate; 50 samples were testate for compatibilities
Conclusions: All methods demonstrated a good performance. The automated reading softest
reactions by DAYmate S were flexible. A few difficult samples were marked as NI due to automate inability of interpretation. Retesting the samples or visual inspection by a technician provided a correct
result.

The first impression of the new system is that it offers a real flexibility in blood grouping, however more timeis needed for a more detailed opinion.

THE IMPORTANCE OF DETERMINING THE EXTENDED PHENOTYPE.

V.Hălmagi, C. Bichiş**, Adina Stanciu**
* CTS Deva , ** CTS Hunedoara

The research of the erythrocytes antibodies is an essential biological analysis for the prevention of the post trasfusional immuno-haemolytic accidents and for the incompatibility of the fetal-maternal diagnosis.
It is important to detect the phenotype, because, according to it, we'll know which antibodies can occur most frequently.
Clinical interest
This research of the irregular antibodies is made:
before transfusion to prevent hemolytic transfusion accident.
after transfusion, to detect any occurence of an antibody of primary immunization, which may disappear later, but still dangerous because reactivation is possible (secondary response) during a subsequent transfusion or pregnancy. Therefore, the rule available for the antibodies, is a dangerous antibody "an antibody for a day remains an antibody forever," a term that summarizes that this antibody, even after it has disappeared (not detected in testing) should always be taken into account in the choice of a transfusion unit.

Pregnant women
It is important to detect all aloantibodies with clinic significance.
Antigen systems of clinical transfusion interest (other than the RH system) Kell system: Duffy system, Kidd system, MNS system, P System, Lutheran system, Lewis system, Cw antigen.
RH Kell phenotype and extended
This must be made to: blood donors, pregnant women during the first months of pregnancy (the first test before the end of the third month) during prenatal testing, female subjects of childbearing age, who should receive transfusions, children, youngs and adults, alo-immunisated patients, potential patients, who will become multiply transfused (cronical- diseases, oncological diseases, hematologic), prospective candidates for transplant.

We conducted expanded phenotype to a total of 500 loyal donors in Hunedoara, to see phenotypes frequency in our population of donors, and the correlation with the frequency in the Caucasian population.

Conclusion

- Perform extensive phenotype is especially important for loyal donors, so that they can be asked to donate especially to multiply transfused ones, which requires transfusion with the same phenotype.
- For this determination to have an end point, it is necessary the detection of the extended phenotype

and inviting especially those who are known to be candidates for repeated transfusion.

THERAPEUTIC APHERESIS.

G. Hanganu, M. Catană, D. Gheorghe, M. Coman, I. Neagu, E. Raduţă, D. Raduţă
CTS Ploieşti

Introduction: Therapeutic plasma exchange is a medical procedure used quite often lately procedure involving increased consumption of FFP. It uses an automatic cell separator, moving large molecules into the bloodstream and unwanted.

Method: Human albumin +/- saline fluid replacement is usual. Fresh frozen plasma can be used in therapeutic exchange in treatment for thrombotic thrombocytopenic purpura. Therapeutic plasma exchange is indicated only for situations where it is obvious benefit to being weighed against the risks.

Erythrocyte/apheresis therapeutics (abnormal red cell replacement) is commonly used to treat sickle cell disease or prevent complications.

A less common use in therapeutic apheresis procedure and platelet apheresis includes Leucytes/ apheresis numeric reducing these cells when their number is extremely high.

Fotoferesis extracorporeal (similar procedure) is used to inactivate T cells is a procedure that uses immune/absorbent column that removes specific antibodies.

Therapeutic plasma exchange removes high molecular, weight substances such as harmful antibodies in plasma. This is usually done using an automated blood cell separator to ensure fluid balance and maintain normal plasma volume. This may require the introduction of femoral or jugular venous lines to enable proper blood flow. Typically, 30-40 ml/kg of plasma are removed at every procedure and replaced with isotonic solution of human albumin 5% (some 25-50% of the substitute service replacement with saline 0.9%).

The exchange made with fresh frozen plasma therapy is reserved for thrombotic thrombocytopenic purpura, or to replace clotting factors. A volume plasma exchange, remove about 66% of a second constituent and intravascular volume plasma exchange about 85%. Therapeutic plasma exchange is normally combined with the usual treatment of the disease, such as immunosuppressive drugs to improve the base.

Indications for therapeutic plasma exchange. This procedure should be performed only when there is evidence of its effectiveness. There are two categories of indications.

Indications Class I: Neurology, Hematology; Renal Syndromes; Metabolic; Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection.

Indications Class II: Neurology; Hematology; Hemolytic uremic syndrome; Alloimmunisation red blood cells during pregnancy; Catastrophic Anti/phospholipid Syndrome; Stroke systemic lupus erythematous

Conclusions: Considering the multitude of therapeutic indications plasma exchange transfusion centers must be continuously prepared with large amounts of PPC can meet these demands.

MEDICAL CHALLENGES IN APHERESIS PROCEDURE WITH MEDICAL INSTRUMENTS.

E. Dumitriu, N. Diniţă, M. Hanta, L. Groza
BTS Focsani

Beckground: The term of „Apheresis" comes from the Greek one „aphairesis", which means „to push away, to get something out of". Apheresis is the procedure through which the blood is separated in its component parts, keeping one or more components and returning the remaining ones to the donor. The procedure is called plasmapheresis (if plasma is donated) or citapheresis (if a cellular component is donated). As standard blood components that are obtained through the separation in a total blood unit have a volume and a cellular concentration that do not match the conventional therapeutical transfusion dose, it has been developed a technology that processes a bigger volume of the donor's blood, in order to obtain bigger quantities of a blood component.

Materials: CTS Focsani uses the automated system of blood gathering Trima Accel 6.0. This is an automated separator of blood cells, which is to be used in blood components donations for further transfusions to patients.

Depending on the set of one-use only tubes that are used, the Trima Accel system can gather: double ACD-A/ AS-3 erythrocytes (deleukocyted or notleukocyted erythrocytes) or the following concentrates – separately or in combinations; platelet apheresis (singular, double or triple units); platelet apheresis, deleukocyted leukocytes, double or triple; plasma, deleukocyted leucocytes; erytrocytes ACD-A/AS-3, leukocytes deleukocyted by using an integrated filter (a filter for gravitational filtration or Auto RBC filter). The Trima Accel system of taking blood components samples, which is either integrated in the sets of one-use-only tubes or is used as an accessory for sterile connection, allows the aseptic extraction of a sample from the platelets bag for further bacterial testing or for other

testing. The system does not interfere with blood fluids that are returned to the donor.

Cases: The research was conducted on a sample of 60 loyal donors, with universally optimum parameters (weight, height, Hb value, platelets). As the reaction of a donor can appear quickly, both Trima Accel system as well as the donor have been monitored during the whole procedure.

Results: After the study, it was revealed that only 5% of the donors had reactions like anxiety, facial and finger paresthesia, hypo-blood pressure. There weren't registered reactions such as hives, syncope, nausea or vomiting. By using Trima Accel, there have been obtained 100% leukoreduced products, ready to be transfused; it has been observed a low risk of external contamination, but also a low risk of contamination through exposing the patient to products combined from multiple donors.

Conclusion: The apheresis method is used at CTS Focsani in order to obtain platelet concentrate, which represents the equivalent of 3 up to 13 standard platelet units.

Platelet concentrates obtained through apheresis have advantages such as: a lower risk of transmission of cytomegalovirus infection, a decrease of post-transfusional nehemolitic febrile reactions, lowering the risk of presensitising which could lead to a lack of response to future platelets administration or to a graft rejection in case of cancer, improvement of post-operator results for patients with heart surgeries, which can be compared to using nonleukoreduced blood products. The disadvantage of automated donation is that it requires expensive equipment and supplies.

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E. Dumitriu, N. Diniţă, M. Hanta, L. Groza
BTS Focşani

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THROMBOTIC THROMBOCYTOPENIC PURPURA – THERAPEUTIC PLASMA EXCHANGE – CASE SERIES.

A. Alexe, I. Dumitru*, I. Voican**, C. Ciufu**, H. Bumbea*, A-M Vlădăreanu***
*Transfusion Department, Emergency University Hospital Bucharest, ** Hematology Department, Emergency University Hospital Bucharest

Introduction: Thrombotic thrombocytopenic purpura (TTP) is a rare and severe disease due to the deficiency of von Willebrand factor (vWf) cleaving protein, ADAMTS-13. In its absence ultra large multimers of vWf are not cleaved appropriately and cause spontaneous platelet aggregates in the microcirculation, especially in the brain, heart and kidneys. This produces platelet consumption, and mechanical fragmentation of erythrocytes causing mycroangioapathic hemolytic anemia.

We report 2 cases of pacients diagnosed with TTP to highlight the importance of first line treatment with plasma exchange and the necessity to have a sufficient fresh frozen plasma (FFP) unit reserve in Transfusion Departments.

Case 1: a 48 y.o. woman presented with metrorrhagias and neurological manifestations (paresthesias, aphasia/disphasia), with platelet nadir 30.000/mcL, hemoglobin =5,5 g/dL and multiple schistocytes on peripheral blood smear. After treatment with plasma exchange there were remission of symptoms and normalization of biological parameters.

Case 2: a 28 y.o. woman diagnosed with TTP during a pregnancy with spontaneous abortion, with a 10 year history with multiple relapses caused by another pregnancy and different infectious episodes, who received combined therapy : FFP infusion, plasma exchange, corticotherapy and monoclonal anti CD 20 antibody. There was an increased number of FFP units needed for the management of this patient as the number of relapses increased.

Conclusion: Once TTP is suspected treatment with plasma exchange must be started as soon as possible given the reported mortality rate of 90% in patients who do not benefit from plasma exchange.

INTRAUTERINE TRANSFUSION.

G. Hanganu, M. Catana, D. Gheorghe, M. Coman, I. Neagu, E. Raduţă, D. Raduţă
CTS Ploieşti

Introduction: Therapeutic solution increasingly used in medical practice, intrauterine transfusion allows mothers immunized RhD, to give birth to children viable even in case of outbreak of hemolytic of the newborn.

Material and method: The most common indication intrauterine transfusion is: red blood cells used for prevention and treatment of fetal anemia due to disease of the fetus and newborn hemolytic or treating parvo/ virus infection, and for neonatal allo/immune thrombocytopenia platelet.

This is an area of high medical specialty that requires a close collaboration between experts in fetal medicine, hematology, laboratory and blood transfusion. Even taking the most serious precautions in case of uterine transfusion, fetal death risk is 1-3% per procedure and subsequent feto/maternal bleeding can cause hemolytic disease of the newborn yet.

The objective of intrauterine transfusion of packed red blood cells is to prevent and treat fetal anemia (fetal hydrops) and aims to continue the pregnancy until the child is viable and can be born (less than 36 weeks gestation). High-risk tasks are monitored through weekly fetal Doppler ultrasound peak systolic velocity scans of the middle cerebral artery, indicating the severity of fetal anemia, fetal growth as well. Fetal blood samples indicated if anemia is severe before 24 weeks gestation, fetal death if specified, or if there is a rapid rise in maternal allo-antibodies.

Clinical guidelines for intrauterine transfusion varies from one specialist to another, but according to data published indication of intrauterine transfusion include a hematocrit below 25% between 18-26 gestation weeks, and below 30% after 26 weeks. Target hematocrit after intrauterine transfusion is usually 45%. Balance between risks and anemia fetal intrauterine transfusions require intrauterine transfusion to be made as late as possible and frequent transfusions are reduced, transfuse amount of red blood cells with maximum efficiency, with a bigger hematocrit. The components are heated to 37° C just prior to transfusion. Leucodepleted irradiated products are mandatory. Neonatal deaths are reported by graft versus host disease, in cases of intrauterine transfusion products irradiated. Children receiving intrauterine transfusion, transfusion should be up to 6 months later only irradiated products.

Qualities of a concentrate of red blood cells for transfusion intrauterine are: Small amount of plasma (H = 70-85%); CPD harvested (without additive solutions that could have a risk of toxicity); Leucodepletion; Maxim harvested 5 days (to avoid hyperkalemia); Anti-CMV antibody negative; With screening for sickle cell disease; Irradiated (to prevent graft versus host disease); Usually group O (titer decreased hemolysis); Rh and Kell D negative erythrocyte antigens without maternal allo-antibodies; Compatible with TCI plasma mother.

Intrauterine transfusions of platelets apply for

autoimmune neonatal thrombocytopenia.
Conclusion: There are good experiences in Europe on intra-uterine transfusion and Romania in recent years began to be practiced successfully in several hospitals in Bucharest and Timisoara. Although it is at first intrauterine transfusion technique seems to expand more and more, being a therapeutic solution for saving mothers immunized.

INTRAUTERINE TRANSFUSION IN FETAL PATHOLOGY. BUCHAREST BE EXPERIENCE.

C. Posea, A. Bălan*, D. Brandabur**, I. Gusi***, D. Goşa**
*BBTC, **CMU Regina Maria, *** Cantacuzino Hospital

Fetal anemia is a serious complication in pregnancy and associated with perinatal mortality and morbidity. The main causes of this condition are red cell alloimmunization, parvovirus B19 infection, chronic fetomaternal hemorrhage, and homozygous alpha-thalassemia. Intrauterine transfusion (IUT) treatment is a successful therapeutic procedure which improves survival of the severely anemic fetus. The selection of blood components for this procedure involves collaboration between physician in charge and blood establishment. The following factors must be considered when transfusing fetus: (1) smaller blood volume, (2) reduced metabolic capacity, (3) higher hematocrit and (4) immaturity of the immune system. There is a significant risk of CMV transmission and graft versus host disease, therefore blood components for IUT must be leucocyte depleted, irradiated and transfused within 24 hours of irradiation. Red cells for IUT must prepared and used by the end of day 5, free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B. The units are cross-matched with maternal blood to reduce the risk of sensitization to new red cell antigens. This presentation focuses on the collaboration between Bucharest Blood Transfusion Center and Obstetrics Departments performing IUT.

HAEMOLYTIC NEWBORN DISEASE. CASE PRESENTATION.

G. Hanganu, M. Catană, D. Gheorghe, I. Coman, I. Neagu, E. Raduţă, D. Raduţă
Blood Bank Ploieşti

Introduction: Maternal immunization due the antigen D, makes many couples who are in the situation that women be immunized, to adopt a restrictive family planning, giving up having children, or limited to having only one child. Thanks to medicine advances, there are couples but also in terms of maternal immunization, have the courage to have one or two children.

Material and method: In 16.05.2015 presents to CTS Ploiesti a female 34 years old, six weeks pregnant, for determining anti D antibody. The research findings unusual irregular antibodies for laboratory practice, as they cause irregular antibodies and identify anti/D antibody in titer of 1/4096, result are very rare in CTS Ploiesti activity.

On the occasion of handing results to the applicant, making the case history, that person is immunized, he had a history of 6 miscarriages in low month, during which, were immunized. Subsequently, even in the context of anti D immunization, already known, the woman born at term, 6 years ago, a relatively healthy child, for this task, being hospitalized in Belgium.

First childbirth took place in a hospital in Belgium, where hemolytic disease of the newborn was treated by transfusions, since fetal life at different times, starting in the fourth month. After birth the child has received another 3 Red cell transfusions to correct anemia, currently being a perfectly healthy baby without hemolytic disease sequel.

Following the earnings received, the pregnant woman decides to go back to Belgium, to be followed during pregnancy. Here the pregnant woman was hospitalized and supervised throughout pregnancy, during which anti D of pregnant women have increased exponentially, reaching 1/16324, pregnant moment in which she was subjected therapeutic plasmaphereses. Pregnant women throughout pregnancy did 30 therapeutic plasmafereses, designed to keep titer antibodies D to 1/4096 and fetus received 6 intrauterine transfusions, which made possible the good evolution until the term of pregnancy, cesarean delivery. Baby birth with normal hemoglobin, 19 mg / dl, which progressively decreased because the maternal antibodies still outstanding, and has subsequently received three transfusions.

At 3 weeks of life hemoglobin child, reached 7 g/dl and after transfusion reached 12 g/dl, and then after 2 months received another transfusion, that from 7 g/dl, reached to 12 g/dl hemoglobin child and the last three months of receiving a transfusion necessary normalization of hemoglobin.

Conclusion: Upgrading medical techniques allow the survival of children who otherwise would have been viable or very high health problems.
It depends on us to have available sufficient blood products to support these special cases: fresh frozen plasma and therapeutic apheresis enough red blood cells leucodepletion on time and with required qualities for babies.

If these techniques are now routine in Europe, and in Romania is a rarity, by doctors' work and through our work, we can change this situation.

HEMOLYTIC DISEASE PREVENTION.

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Introduction: Suppression of maternal immunization by blocking the immune response mayor or seizure and destruction of extravascular red blood cells D positive practiced efficiency since 1970 by injecting "anti-D immunoglobulin" derived from the plasma of donors immunized against the antigen D. Generalizing this prophylaxis was a breakthrough, but after nearly half a century, the results are far from satisfactory. The main reason is not lack of efficacy, but the fact that prevention is not applied correctly.

Material and method: Allo-immunization prevention against a specific antigen D must be implemented strictly to any woman Rh negative, non-immunized anti-D Rh and a positive child will be born. Maternal immunization requires a "contact" between blood group antigen and mother "reactive" that does not have this antigen. The only possibility for a Rh negative woman to immunize is pregnancy or Rh incompatible blood transfusion.

Switching fetal red cells in maternal circulation is well known. This fetal cell from maternal blood was demonstrated by Kleihauer or by flow cytometer, techniques that can be made from week 10-11 of gestation.

The frequency of bleeding fetal maternal depends on the situation normal gestational age: it appears in the first trimester of pregnancy to about 4% of pregnant women increases from 12% in the second quarter, 45% in the third quarter and to 60 % at birth. Injection of "anti-D immunoglobulin" must necessarily be applied in any Rh negative woman in case of non-immunized: Late abortion; Ectopic pregnancy; Medical termination of pregnancy; Trophoblastic biopsy; Amniocentesis; Puncture of fetal blood; Circulate cervical; Change maneuvers version; Death in utero; Pelvic surgery; Reduction of embryos; Placenta praevia,; Bleeding; Abdominal trauma. Injection of "anti-D immunoglobulin", must be performed within 72 hours at the latest after birth because of a dose of 100 mg I.V. ii correspond to a test Kleihauer < 5 fetal RBC / RBC 10,000 adult; the dose should be adjusted by the fetal-maternal hemorrhage. The protocols include administration antepartum (28, 34 weeks of amenorrhea) indicate further reducing the incidence of immunization in 0,1-0,2%. There is in this regard: D immunoglobulin anti exclusively intra-muscular administration, D immunoglobulin anti intravenous or intramuscular at a price high enough.

Conclusion: Immunoglobulin needs require a collective effort to be able to source assure rich plasma anti-D antibodies from immunized trans-placental women.

Prevention correct significantly reduces frequency of Rh negative mother's allo/ immunization with children Rh positive. Return the discussion need to occur in Romania and stable blood products, plasma fractionation native.

At the beginning of the third millennium, lack of preventive immunization antigen Rh D negative women can be considered as a serious medical malpractice.

THE ROLE OF HLA LABORATORY IN TEH SELECTION OF THE BEST HEMATOPOIETIC STEM CELL DONOR.

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Hematopoietic stem cell transplantation represents a therapeutic potential currative alternative currently used in the treatment of many malignant and non-malignant diseases. One of the essential conditions for a successful hematopoietic stem cell (HSC) graft is to identify, in a timely manner, the best HSC donor. In the process of donor selection should be taken into account several aspects. The classical medical criteria such as the degree of HLA compatibility, sex, CMV status, weight, blood group, remain the defining criteria in the selection of the donor. However, a very important role is also the optimal timing for transplantation, depending on the progression of the patient disease. To achieve this, it is necessary to start the search for a donor as soon after diagnosis, particularly in high risk cases. The search in the family provide a compatible donor HLA 10/10 in 20-25% of cases, for the rest beeing necessary to start the search for a compatible unrelated donor. The frequencies of HLA alleles and their linkage disequilibrium patterns differ significantly among human populations. The alleles and haplotypes frequencies in some major registries have been published for their own populations. HLA testing of all first-degree relatives available makes it possible to identify patient`s haplotypes, based on the transmission of genetic characters in the family. This will allow to estimate the chances of finding, quickly or timely, a donor 9/10 or 10/10 HLA compatible and orientates the search towards certain registers and / or certain populations. It also allows the identification, from the beginning, patients with minimal chances for finding an unrelated donor with a suitable HLA compatibility. In

these cases, selecting a haploidentical donor from the family, available immediately / in the best time for transplantation, may be a preferable option in selected cases.

THE EXPERIENCE OF HLA LABORATORY IN A SEVERE POST- TRANSFUSIONAL REACTION-CASE REPORT.

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Severe post-transfusion reactions require immediate recognition, a complex laboratory investigations and a good clinic condition. The transfusions must be izogroup, izoRh. In case that we suspect such of incidence in transfusion, it s stopped the administrarion of these and take the proper treatment. The study is based of the experience of HLA Laboratory to investigate the immunization against the leucocyte antigens. So, a patient with VHC cirosis from Institute Fundeni developed a severe post-transfusion reaction after a perfusion with PPC AII izogroup, izoRh. The post-transfusion reaction was a n acute pulmonary edema.

The authors discuss the complex protocol to investigate the post-transplant reaction.The immunohematological tests show the absence of allo-antibodies anti-erytrocytes in the serum of the patient and plasma of the donor. The detection of anti HLA antibodies together with the HLA fenotype of the recipient and donor were performed.

The authors discuss the results, highlighting the possible role of anti HLA antibodies in triggering transfusion reaction.

VIRAL LOAD DISTRIBUTION IN HIV-1 INFECTED BLOOD DONORS.

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Background: Introduced as a complement to serological testing Nucleic Acid Amplification Techniques (NAT) are an important tool in reducing the residual risk of TTI (Transfusion Transmitted Infections) due to their capacity to detect serological window or silent chronic infections. NAT is also considered as a replacement for immunoblots in the confirmation algorithms offering the direct proof of the infectious status of the pacient. In Romania, blood donation screening for TTI relies on serological methods and previously reported data point to the need of introducing NAT. We report here the results of NAT testing on serologically confirmed HIV-1 positive donors and evaluate the potential benefit of adding this technique to serological confirmation. The resulting viral load distribution can contribute as well to establishing the right size of „mini-pools" for NAT screenig of donations.

Methods: 352 plasma or serum samples from 327 anti- HIV-1 confirmed donors, resulted after sreening of 2475127 donations during 2010-2015, were extracted with EZ1 DSP Virus Kit (Qiagen) and amplified with Arthus HIV-1 RG RT-PCR kit (Qiagen) for viral load quantification (VL). The test has an LOD 95%(Lower limit of detection with a probability of 95%) of 67 IU/ml The current algorithm for serological confirmation includes a second line combined Ag-Ab EIA, a p24 HIV-1 Ag test and Inno-Lia Score (Fujirebio). Follow-up is recommended for samples with equivocal results.

Results: 342/352(98.9%) samples had detectable RNA with a log c over 1.8 which coresponds to LOD 95%. 6 samples were repeatedly detected under the LOD 95% and 4 samples were not detected at all, either due to the limits of the test or to originating from so called „elite controllers". 91% VLs were over log 3.0 which allows easy detection over LOD95% in pools up to 6 donations. 8% were over log 6.0, cumulating 78% of the seroconversion samples as compared to 10% among VLs under log 5.0 which represent 89% of all viremic samples. VL concluded the diagnosis in 8 cases with equivocal serological results and 4 seronegative repository samples from previous donations given by repeat donors.

Conclusions: The results underline the need for NAT screening of all donations and addition of VL determination to the current confirmation algorithm in order to interdict window-period donations and reduce the delay in final diagnosis for cases with inconclusive serological results, respectively. Establishing the adequate size of „mini-pools" has to considere the local prevalences an incideces of HIV infection, the VLs in seropositive donors and the impact on the blood unit validation process. The existence of seropositives with undedectable VLs, reported worldwide, indicates that this technology cannot exclude the serological screening even with NAT screening on individual donation, as its aim is to reduce the residual risk of TTI due to window-period donations.

FREQUENCY OF HBV AND HCV INFECTIONS AMONG BLOOD DONORS WITH ELEVATED ALT LEVELS.

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Background: Introduced as a suroggate test, toghether with anti-HBc testing to minimize the risk of post tranfusion hepatitis in an era when HCV was unknown and sensitivities of HbsAg tests were far from the present, ALT determination is nowadays under debate and has been discontinued in many blood services for causing unnecesary loss of blood products and deferral of otherwize eligible donors. Sceening of blood donations in Romania does not include anti-HBc testing and Nucleic Acid Amplification Techniques (NAT), therefore excluding ALT from the pannel of tests needs a serious consideration. In a previous study we have reported a window period HCV infected donation interdicted among other 3464 excluded based on high ALT levels. The aim of this study is to reevaluate the role of ALT testing in preventing HBV and HCV transmissions after the introduction of more sensitive screening tests.

Methods: During 2010-2015, 5270 donations were reported with abnormal ALT values in Bucharest Blood Transfusion Center, discarded and sent for supplemental testing which included second line screening tests for HBsAg and anti-HCV, anti-HBc and anti-HBs. Follow up for three months was recommended for cases with elevated ALT.

Results: 34 donations were positive for HBsAg, 181 for anti-HCV and 2 were HBV+ HCV coinfections, with an overall rate of active infection of 4.1%. HCV infections accounted for 83.4% of all active infections and 2/5 recent HCV infections were serologicaly detected by combined tests only. Past HBV infection was demonstrated in 15.1% cases, 8.14% lower than the frequency previously reported, and 80.8% were negative for HBV and HVC infection markers. Though recommended for all donors with elevated ALT values follow up was available in 35.3% only and among them seroconversions as well as evolutive titers for anti-HBc and anti-HBs were evidenced in 11 and 36 cases respectively, indicating second window and recently resolved HBV infections.

Conclusions: : HCV is the most prevalent among active infections and better detection of recent HCV infections by combined tests minimizes the contribution of ALT testing in preventing HCV transmission. The rate of active and past HBV infection has declined over the last years, especialy in young blood donors due to vaccination programmes, but incident infections still occur and in the absence of NAT and anti-HBc screening of donations ALT testing remains a supplemental tool that can excludes HBV transmission during serologic window periods. Follow up of all cases might result in a higher frequency of incident cases interdicted by ALT determination.

SEROLOGICAL AND VIROLOGICAL CHARACTERISTICS OF HCV INFECTION IN BLOOD DONORS.

A. Necula
NIHT Bucureşti

Background: Detection of HCV infection relies on serological methods and Nucleic Acid Amplification Techniques (NAT) have been developed to distinguish active from inactive or past infection, and to detect serological window or silent chronic infections. Particularly in blood donors, which are apparently asimptomatic carriers, the serological diagnosis is very challenging since serological profiles profiles resulted from weak and/or incomplete response to viral antigens are frequent, suggesting inactive or past infection, as well as nonspecific reactivity. We report here the results of NAT testing on samples with different anti-HCV serological profiles in an attempt to evaluate its contribution to the confirmation algorithm as a complement to serological methods and the yield of combination screening tests.

Methods: Donations are screened with a combined Ag-Ab HCV enzyme immunoassay (EIA) and reactive donations are referred for confirmation. The current algorithm for serological confirmation includes a second line combined Ag-Ab EIA, an anti-HCV EIA and Inno-Lia Score (Fujirebio) anti-HCV immunoblot. Follow-up is recommended for samples with equivocal results. According to the confirmation algorithm 2469 reactive samples resulted from the sreening of 2074842 donations during 2012-2015 qualified for analysis in immunoblot and 1297 of them were available for extraction with EZ1 DSP Virus Kit (Qiagen) and viral load quantification with Arthus HCV RG RT-PCR kit (Qiagen). The test has an LOD 95%(Lower limit of detection with a probability of 95%) of 34 IU/ml.

Results: Strong positive, weak positive, indeterminate and negative profiles were obtained in 81.8%, 6.9%, 8.6% and 2.7% cases respectively. NAT was performed on 917(45.5%), 167(97%), 166(78%) and 47(69%) samples from each category. Strong positive profiles were associated with 75% detectable RNA while in the weak positive, indeterminate and negative categories only 12%, 9% and 17% of the samples had detectable RNA respectively. All the viremic samples with negative antibody serology represent the yield of the combination screening tests and are window period samples. Weak positive and indeterminate samples with detectable RNA were also from donors with recent infections. The apparent low yield of NAT among these last categories is due to the frequent association of these profiles with past infection.

Conclusions:The use of combined tests in screening

donations for HCV interdicted 10 infectious donations (1/ 207484) undetectable by previously used anti-HCV tests. As a complement to serological confirmation NAT testing is a valuable tool in solving cases with equivocal results, particularly HCV infections identified by combined screening tests. The rate of HCV RNA detection among samples with anti-HCV strong positive profiles is comparable to those reported for in other european countries indicating the ratio of inactive or past infections. On the other hand, the existence of NAT negative HCV serologically positive blood donors has been reported worldwide pointing to maitaining the serological screening evan with the most sensitive NAT performed on Individual Donation.

CAUSES OF DEATH IN THALASSEMIA MAJOR, RETROSPECTIVE AND PRESENT.

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NITH Bucureşti

Introduction. Beta thalassemia major is a genetic blood disease characterized by severe anemia and addiction of the chronic administration of blood (2-3 weeks). As a result of advances in the treatment of this disease was significantly improved lifespan and quality of life of these patients.

Material and method. The study was carried out on patients hospitalized in the INHT, over a period of 20 years, from 1996 to 2015, on the mortality and causes of death.

Results. If before 1995 death was situated predominantly in the second decade of life, around 60% of deaths due to complications haemosiderosis post-transfusion, main cause of death is cardiac complications (76%) after 2010 profile cases of death was change, the frequency of death by cardiac complications is lower with the emergence of new cases.

Conclusions. Due to increasing lifespan and quality of life, through correct transfusion and iron chelation treatment, causes of death in thalassemia major are not specific chronic anemia or iron overload in the body.

IRON OVERLOAD IN POLITRANSFUSED THALASSAEMIA MAJOR PATIENTS-CORRELATION BETWEEN IMAGISTIC METHOD AND SERUM FERRITIN LEVEL.

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Introduction. The main cause of mortality in major thalassaemia remain iron overload that induced cardiac failure and liver, pancreas and other organs progressive damage. Early chelation therapy can prevent these complication, so early detection of iron overload is crucial.

Nowdays iron overload can by monitorized noninvasively by serum ferritin levels and by magnetic resonanceT2* and FerriScan. Regular monitoring with serum ferritin can provide useful information about iron overload, but is not a very sensitive method, infection, inflamation and hepatic disease can cause false increase in level. FerriScan is a non invasive liver iron concentration test and offers a safe, fast and most accurate determination of liver iron levels.

Method. There are 104 patients with major thalassaemia in transfusion and chelation therapy registred in NITH. Serum ferritin levels are every 3 month determinated for each patient. By Ferriscan iron overload is monitorized for 50 patients.

Results. In october-december 2014 were invastigated 18 patients by Ferriscan , results obtain are:6 patients low level LIC, 4 patients medium level LIC and 8 patients severe overload. Second Ferriscan determination was in april-june 2016 for 36 patients: 21 of them with low level LIC, 10 with medium LIC and 5 patients with sever iron overload; 4 patients were reevaluated by Ferriscan after intensification of chelation therapy. We observe that LIC value>15 mg/g dry tissue were associated with serum ferritin level above 2000ng/ml.

Conclusion: For a better evaluation of iron overload is mandatoty to have an imagistic method available in Romania, helpful to adjust chelator doses and prevent iron overload complication and medication toxicity.

ANAEMIC SYNDROME IN INFANTS AND CHILDREN AGED 1-3 YEARS. CASES OF THE NATIONAL TRANSFUSION HAEMALOLOGY INSTITUTE.

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Purpose of the study: We have studied the anaemic syndrome in infants and children aged 1-3 years, and we have also performed certain correlations between anaemia and feeding of the children.

Material and method: We have studied a number of 358 children under 3 years of age (27 infants and 331 children aged 1-3 years), surveyed throughout a period of 3 years (3013 – 2016)) in Laboratory of haematological Institute. In these children we have considered the following parameters: complete blood cell count (haemoglobin, haematocrite, MCV, MCH, MCHC, peripheral blood smear), serum iron and, when

possible, haemoglobin electrophoresis and osmotic resistance test.

Results: Out of the 358 children, 195 were boys (56,14%) and 163 girls (43,86%).
We have established the following etiologies:
1). 148 cases (41,34%) – iron deficiency anaemias due, in most cases, to deficient feeding and, also, often combined with lack of vitamins (A, C, E and complex B vitamins); most of these children had received nothing else but milk (either breast-milk or „formula") up to 6 month of age, and they have received food rich in iron very late, even al 7-8 month of age. Most of them had slight forms of anaemia (Hb. over 10 g./dl.) or moderate anaemia (Hb. between 9-10 g./dl.), but we had 6 cases of severe iron – deficiency anaemia, with Hb. below 8 g./dl., cases that required prolonged therapy with high doses of iron, and also vitamin supplements.
2). 191 cases of β-thalassaemia minor, 1 case of α-thalassaemia minor, 1 case of δβ- thalassaemia minor and 4 cases of Lepore-haemoglobinopaty (totally 55,64%); 78 of these children also had iron-deficiency; we also took into account the fact that the iron-deficiency could mask a β-thalassaemia minor, and also of the possible physiological persistence of foetal haemoglobin (Hb.F) in small children, even after 1 year of age.
3). Other cases: 12 cases with hereditary spherocytosis (3,34%) adn 1 case with glucose-6-phosphate dehydrogenase deficitary.

Conclusions: Anaemia in children under 3 years of age is still a very freqvent clynic condition. Deficient feeding is the cause of most of the cases of iron-deficiency or vitamins-deficiency anaemias, even in families with a good socio-echonomical level. Besides, at this age, we can discover cases of haemolytic congenital anaemias, such as thalassaemia and spherocytosis. These conditions can often be associated.

REVIEW CRITERIA FOR QUALITY DOCUMENTS DUE TO THE IMPLEMENTATION OF THE NEW COMPUTER PROGRAM OF BLOOD TRANSFUSION CENTERS.

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Introduction. From 20/1/2016 began to be put into practice in all transfusion centers in the country the new computer system for managing blood donors and the reserve of blood and blood components, conducted by INHT through a project begun by the financing contract concluded with the Ministry of Communications and Information Society.

The overall objective of this project was increasing the efficiency and quality of blood donation activities at the national level, by developing a new computer system in the national blood transfusion system.

Working method. The implementation of this new program involved not only donors input into the new system but also to adapt national quality documents (SOPs) to the new working procedure.

In this context refers firstly to review SOPs on the Education Recruitment and Collecting blood department, because here the first changes of the working procedure had occured. Some procedures were modified: at the reception of donors (SOP Identification of donors, SOP Preparation and issue of donor file) which appear the first benefits by introducing and data verification of donors in the new national database, no longer restricted accepting donors from other counties, the possibility to check clear their identity by consulting the database from Population records or National Administration of Penitentiaries; before donation laboratory (SOP Sampling before donation); medical examination (SOP Donors interview, SOP Medical examination, SOP Sorting of potential donors before collecting blood) - here the doctor at each donation can enter the preliminary results of all checks and his personal observations about each of the problems occured; all this will be found at the next presentation of the same donor; collecting hall (SOP Registration and donation qualification).

The Storage, Distribution and Transport department (SOP Delivery of blood and blood components, SOP Blood /blood components stock limits) is also influenced by the new system.

Conclusions. With all the inertia of starting this new computer system implemented, this project already brings significant benefits to business of INHT and transfusion centers in the country by the possibility of retrieving data from a donor anywhere in the country, with the possibility to check exactly also external information systems by allowing retrieval medical history and history of donations, which decreases the risk of accepting a potential donor who don't satisfies all criteria for acceptance, so the risk of spoilage. The system also enables quicker reporting the stock of blood and blood components.