From the editor-in-chief

Dear Friends,

It is our honor and pleasure introduce you the official journal of the Armenian Association of Hematology and Oncology. We named it “Blood and Cancer Secrets”, cause there are so many secrets in hematology and oncology and we want to see them all resolved...
Hope our journal will become your good friend and we will do our best to not disappoint you...

Yours,
Abstracts of the
1st Taiwan-Armenian Medical Conference
THE RECENT ADVANCE TREATMENT AND DIAGNOSIS OF THALASSEMIAS IN TAIWAN
Ching-Tien Peng MD, MPH1,2

1. Children’s Hospital of China Medical University, Taichung, Taiwan
2. Department of Biotechnology, Asia University, Taichung, Taiwan

This island of Taiwan is located about 100 miles off the southeast coast of Mainland China and currently has a population of over 23 million consisting of four main ethnic groups. The largest is “Min-Nan” with 13 million people; they started to move from Fukien Province on the Mainland, directly across from Taiwan, about 300 years ago. The second largest ethnic group in Taiwan is the “Hakka” of six and half million people who first arrived about 150 years ago from Guangdong Province. The third largest group consists of people from all over Mainland China who arrived in Taiwan in the years following World War II. Such “Mainlanders” comprise over 3.7 million people. The fourth largest group in Taiwan is the Native Taiwanese Aborigines, totaling almost six hundred thousand (600,000) closely related to the Malays.

Carrier frequency of β-thalassemia is currently estimated at 2-3%, number of β- thalassemia major patients in Taiwan around 500. Thea-thalassemia carrier rate is 4% (Table 1). And 15-20 hemoglobin variants, most of them are stable types. A few of them are unstable variants like Hb-C and E, coming with the influx of foreign brides from Southeast Asia (Table 2). For treatment of patients, Taiwan is divided into three regions. The northern region’s main facilities are located at National Taiwan University, MacKay Memorial and Chang Gung Memorial Hospitals in Taipei. Patients in the central region are treated at the China Medical University & Hospitals in Taichung. The southern region’s main facilities are located at National Cheng-Kung University Hospital in Tainan, Kaohsiung Medical University and Chang Gung Memorial Hospital in Kaohsiung. Stem cell transplant, including bone marrow, peripheral and umbilical blood stem cell transplantation, is available in National Taiwan University, China Medical University, Chang Gung Memorial and Cheng Kung University Hospitals. The disease-free survival after SCT for thalassemia is 80%, with graft rejection the major cause of treatment failure.

In the year 2012, 19,217 people were diagnosed with or suspected of thalassemia. Among these, 510 were diagnosed as thalassemia major. On the average, each visited doctors 30 times a year. Among these patients, 188 have ever been hospitalized, 454 received regular blood transfusion therapy (1.48 blood transfusions per month and 48.3 units of packed RBC per year). That same year, 423 of 454 patients underwent iron chelation therapy, of whom 216 (51%) received oral Exjade; 131 (31%) oral Deferiprone (L1) medication and 67 (16%) synergistic/additive/rotatory use of L1 and Desferioxamine (DFO), only 9(2%) still received DFO infusion therapy. Of the total 510 thalassemia major patients, 15 received bone marrow and 41 received umbilical blood stem cell transplantation.

Taiwan has two major β-thalassemia organizations. The Thalassemia Association of ROC centered in Taipei and chaired by Dr. Lin Kai-Hsin, consists of patients, their families, and doctors. Another large
group is Taiwan Thalassemia Association (TTA), located in Taichung, chaired by Mr. Shu-Chen Wei and consisting entirely of patients and their families. It was founded in 1992 by a group of volunteers and became an official member of TIF in 1995. TTA usually makes public announcements to promote awareness of important issues in thalassemia, urging patients to get proper treatment with regular blood transfusions and effective chelating program.

Treatment history of β-thalassemia major in Taiwan divided into three periods. In the first (1957-74), patients rarely received adequate blood transfusions, and treatment quality was very poor. During 1975-94, Taiwan’s economy markedly advanced, which spurred the development of thalassemia major treatment centers and treatment quality. Patients had better treatment protocol and far better results. From 1994 to the present, owing to universal health care for citizens of Taiwan by the National Health Institute (NHI) that guarantees health care, patients get comprehensive treatment that provides close monitoring of physical development, medication, X-ray, surgery, laboratory tests inducing hemoglobin electrophoresis and DNA analysis for diagnosis and blood transfusion, even stem cell transplantation also covered by NHI. Blood transfusions procedure to improve quality and safety conforms to international standards, with all kinds of RBC products (like washed, frozen, cryopreserved, radiated and leuco-reduced RBCs) available. Beyond that, patient compliance is the main concern.

Current data regarding specific mutations of β-globin genes in Taiwan are well documented. In our previous study, C to T substitution at nt 654 of IVS-2 was most common in Taiwan. Frame-shift codon 41/42 (4 nucleotides) and A to T substitution at nonsense codon 17 are likewise frequently detected. These mutations of β-thalassemia comprised 91.3% of all cases. Spectra of mutations are similar between Min-Nan and Hakka populations but not found among aborigines (Table 3).

Transfusion-associated infectious diseases form another major concern. Patients are monitored for HIV, plus hepatitis-B and -C annually. No β-thalassemia patient in our group tested HIV-positive; two of sixty were HbsAg-positive. Low infection rate may reflect a nationwide hepatitis-B vaccination starting in 1988. Approximately half of the β-thalassemia group tested positive for Anti HCV-Ab. Carrier rate of HCV in Taiwan is about 0.93%, yet liver function, ferritin concentration and/or pathological abnormality between Anti HCV-Ab-positive/negative patients were not significantly different. Nonetheless, due to HCV’s long incubation periods, continued monitoring is needed to ensure the health of such patients. The final national program of preventive measures by health agencies of government since 1994 included population screening for detection of β-thalassemia carriers, especially before marriage (charge of US$50, reimbursed by the government), health education, genetic counseling and prenatal diagnosis (US$80). Abortion for thalassemia major is legal in Taiwan. The capacity of the above-cited hospital sustained such enormous responsibilities. To reduce voluntary pregnancy termination owing to affected fetus, pre-implantation or pre-conception genetic diagnosis has been initiated for detecting thalassemia in several of these centers.
Table 1. Frequency of α-thalassemia mutations in Taiwan

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>αα/-SEA</td>
<td>82.7-87.4%</td>
</tr>
<tr>
<td>αα/-Fil</td>
<td>5.8-7.2%</td>
</tr>
<tr>
<td>αα/-Thailand</td>
<td>0-3.9%</td>
</tr>
<tr>
<td>αα/α-3.7</td>
<td>0.8-7.9%</td>
</tr>
<tr>
<td>αα/α-4.2</td>
<td>0-0.5%</td>
</tr>
<tr>
<td>αα/ααQS</td>
<td>0-2%</td>
</tr>
<tr>
<td>αα/ααCS</td>
<td>0-0.5%</td>
</tr>
</tbody>
</table>

Table 2. Hemoglobin variants found in Taiwan

<table>
<thead>
<tr>
<th>Hemoglobin variant</th>
<th>Position</th>
<th>Amino acid change</th>
<th>Codon change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb E</td>
<td>B26</td>
<td>Glu - Lys</td>
<td>GAG – AAG</td>
</tr>
<tr>
<td>Hb Constant Spring (CS)</td>
<td>A142</td>
<td>Ter – Gln</td>
<td>TAA – CAA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>termination at codon 173</td>
<td></td>
</tr>
<tr>
<td>Hb Quong Sze</td>
<td>A125</td>
<td>Leu – Pro</td>
<td>CTG – CCG</td>
</tr>
<tr>
<td>Hb Siriraj</td>
<td>B7</td>
<td>Glu – Lys</td>
<td>GAG – AAG</td>
</tr>
<tr>
<td>Hb Kaohsiung (New York)</td>
<td>B113</td>
<td>Val – Glu</td>
<td>GTG – GAG</td>
</tr>
<tr>
<td>Hb G–Honolulu (Chinese)</td>
<td>A30</td>
<td>Glu – Gln</td>
<td>GAG – CAG</td>
</tr>
<tr>
<td>Hb G–His–Tsou</td>
<td>B79</td>
<td>Asp – Gly</td>
<td>GAC – GGC</td>
</tr>
<tr>
<td>Hb G–Hsin–Chu (G–Saskatoon, Coushatta, Taegu)</td>
<td>B22</td>
<td>Glu – Ala</td>
<td>GAA – GCA</td>
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<tr>
<td>Hb G–Szuhu</td>
<td>B80</td>
<td>Asn – Lys</td>
<td>AAC – AAG</td>
</tr>
<tr>
<td>Hb G–Taichung</td>
<td>A74</td>
<td>Asp – His</td>
<td>GAC – CAC</td>
</tr>
<tr>
<td>Hb G–Taipei</td>
<td>B22</td>
<td>Glu – Gly</td>
<td>GAA – GGA</td>
</tr>
<tr>
<td>Hb Queen</td>
<td>A34</td>
<td>Leu – Arg</td>
<td>CTG – CGG</td>
</tr>
<tr>
<td>Hb J–Kaohsiung</td>
<td>B59</td>
<td>Lys – Thr</td>
<td>AAG – ACG</td>
</tr>
<tr>
<td>Hb J–Meinung (J–Bangkok, Korat)</td>
<td>B56</td>
<td>Gly – Asp</td>
<td>GGC – GAC</td>
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<tr>
<td>Hb J–Taichung</td>
<td>B129</td>
<td>Ala – Asp</td>
<td>GCC – GAC</td>
</tr>
<tr>
<td>Hb J–Wenchang wuming</td>
<td>A11</td>
<td>Lys – Glu</td>
<td>AAG – CAG</td>
</tr>
<tr>
<td>Hb J–Ube-2</td>
<td>A68</td>
<td>Asn – Asp</td>
<td>AAC – GAC</td>
</tr>
<tr>
<td>Hb Koln</td>
<td>B98</td>
<td>Val – Met</td>
<td>GTG – ATG</td>
</tr>
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Table 3. Frequency of β-thalassemia major mutations in Taiwan

<table>
<thead>
<tr>
<th>Mutation site</th>
<th>This study (central Taiwan)</th>
<th>Northern Taiwan (Lin et al. 1991)</th>
<th>Southern Taiwan (Chiou et al. 1993)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Min-Nan</td>
<td>Hakka</td>
<td>Mainlander</td>
</tr>
<tr>
<td>IVS-2 nt 654 (C→T)</td>
<td>(β^654)</td>
<td>21</td>
<td>9</td>
</tr>
<tr>
<td>Codons 41/42 (− TCTT)</td>
<td>(β^41/42)</td>
<td>21</td>
<td>7</td>
</tr>
<tr>
<td>Codons 17(A→T)</td>
<td>(β^17)</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Codons 71/72(+A)</td>
<td>(β^71/72)</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>−28 (A→G)</td>
<td>(β^28)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Codons 27/28 (+C)</td>
<td>(β^27/28)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>IVS-1 nt 1 (G→T)</td>
<td>(β')</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IVS-1 3’ end (TAG→GAG)</td>
<td>(β'3’end)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>−29 (A→G)</td>
<td>(β^29)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>19</td>
<td>5</td>
</tr>
</tbody>
</table>

GENETIC SCREENING AND PRENATAL DIAGNOSIS OF THALASSEMIAS AND HEMOGLOBINOPATHIES IN TAIWAN TODAY

Ching-Tien Peng, Su-Ching Liu, Chien-Yu Lin, Chang-Hai Tsai

Department of Pediatrics, Children’s Hospital, China Medical University & Hospital, Taichung, Taiwan; Bureau of Health Promotion, Department of Health, Thalassemia Laboratory, China Medical University Hospital, Taichung, Taiwan; Department of Biotechnology, Asia University, Taichung, Taiwan

Taiwan is 100 miles off the southeast of China with a population of about 23 million people. The α-thalassemia carrier rate is about 4%, β-thalassemia around 2~3% and 15 to 20 hemoglobin variants have been found which are mostly stable with a few unstable types (hemoglobin C, E, & Tak). There are currently about 400 thalassemia major patients who receive regular therapy. Taiwan has had a national prenatal screening program for detecting thalassemias in pregnant women since 1993. There is an average of 350-400 fetuses screened in this way per year in 6 medical laboratories. The main diagnostic procedures are by DNA study of the samples obtained from chorionic villus or amniotic fluid cells. Between 1998 and 2011, prenatal diagnosis procedures for identifying thalassemias and hemoglobinopathies were performed on 1240 fetuses which were at-risk for α-hydrops and β-thalassemia major in one central Taiwan medical center. The data shows: 17% of the fetuses were at risk of α-hydrops, 4% for β-thalassemia major and
2 fetuses for β/E-thalassemia, resulting in early prenatal diagnosis and termination of pregnancies affected with homozygous α-hydrops and β-thalassemia major in this area. Ten percent of the 1240 fetuses were at risk of compound heterozygosity of β-thalassemia and abnormal hemoglobin of the β chain, and 8 different β-thalassemia mutations have been found. Four mutations, IVS-II-654 (C>T), codons 41/42 frameshift (-TCTT), and nonsense codon 17 (A>T) and codon -28 (A>G), account for more than 95% of mutant alleles. Hb E [β26(B8)Glu→Lys, GAG>AAG] was found to be the most common Hb variant at about 0.5-1%. There are 3 genotypes of α(0)-thalassemia 1 and at least 6 of α(+) -thalassemia 2 in these specimens. The most common types of α(0)- and α(+) -thal were the SEA deletion and the -α(3.7) rightward deletion, with frequencies of 87.79 and 4.85%, respectively. The results of this study provide a reference for designing a locally relevant antenatal diagnostic test for controlling the spread of thalassemia. The program’s success is indicated by the 70% reduction in the number of newborns affected with β-thalassemia major. Moreover, in order to reduce the choice of interrupting the pregnancy in case of affected fetuses, preimplantation or preconceptional genetic diagnosis has been set up for thalassemias in several centers of Taiwan.

PREVALENCE AND PROGNOSTIC VALUE OF TET2 GENE POLYMORPHISMS IN CHILDHOOD ACUTE MYELOID LEUKEMIA IN TAIWAN

Meng-Ju Li, MD1, Yung-Li Yang, MD2, Shiann-Tarng Jou, MD3, Meng-Yao Lu, MD2, Hsiu-Hao Chang, MD2, Kai-Hsin Lin, MD2, Dong-Tsamn Lin, MD2 and Ching-Tien Peng, MD, MPH4

1. Department of Pediatrics, National Taiwan University Hospital Hsin-Chu Branch
2. Children’s Hospital of China Medical University & Hospitals, Taichung, Taiwan
3. Department of Pediatrics, National Taiwan University Hospital and College of Medicine, National Taiwan University, Taipei, Taiwan
4. Department of Pediatric Hematology and Oncology, Children’s Hospital of China Medical University & Hospitals, Taichung, Taiwan

Introduction

Acute myeloid leukemia (AML) is a phenotypically and genetically heterogeneous disease, accounts for 10% of childhood leukemia. The prognosis of children with AML has improved greatly over the past 30 years, and the Taiwan Pediatric Oncology group (TPOG) AML 97A and B protocols had been designed and explored in 1997 for the treatment of AML in Taiwan with complete remission (CR) and overall survival (OS) rates as high as 80–90% and 50–60%. In recent years, molecular research identified an increasing panel of genetic markers in AML, enhancing better risk stratification, modify
treatment strategy and improving prognosis. The tet oncogene family member 2 (TET2) gene, a candidate tumor suppressor gene, and the mutations are found in adult AML with prevalence of around 10-20% and is associated to prognosis. However, the report in childhood AML is limited. Here, we assess the prevalence of TET2 gene alterations in childhood AML and to identify its association with prognosis.

Method

We enrolled children who were diagnosed AML and visited national Taiwan university hospital between Jan, 1997 to June, 2010. The patients with APL (acute promyeloid leukemia) were excluded due to different treatment protocol. All the children were treated by TPOG AML 97 protocol. The induction therapy consist two courses of cytarabine (Ara-C) and idarubicin (IDR). Patients who achieved CR subsequently received four courses of consolidation therapy consisted of high-dose Ara-C and mitoxantrone or etoposide. The clinical characteristics, such as age, sex, laboratory data, cytogenetics information, relapse, survival time were all collected from TPOG database. DNA was isolated from bone marrow cells at diagnosis and sequence analysis was carried out for TET2 gene. The all data of eligible cases will be collected and analyzed for estimating EFS (event free survival), and OS (overall survival). Survival curves will be estimated by the Kaplan-Meier method. Comparisons were made by Chi-square test for binary variables and t test for continuous variables. For all analyses, the P-values were two-tailed, and a P < 0.05 was considered statistically significant.

Results

Total of 56 pediatric AML patients were enrolled. The mean age is 9.07 ± 5.4 (0.01~17.54) years. There are 34 (60.7%) males. Twenty-four (42.9%) patients had relapse and the overall survival rate is 44.6% (25/56). In this study, there was no nonsense or frameshift mutation, which is frequently identified in adult AML. Total 44 patients (78.6%) present TET2 SNP (single nucleotide polymorphism) and the details are listed in Table 1. There are 18 SNP, and 3 of them (rs72224084, rs58201766, rs59046770) are located in intron. Other 15 SNP are all located in exon. Most of them are located in exon 3 (27 events) and exon 11 (32 events). Only SNP rs3733609 is located in exon 9, and this is synonymous mutation. There are 9 SNP located in exon are not reported in reference yet. Among these, 4 SNP is synonymous mutation. All SNPs are heterozygous, except 4 SNP are homozygous, which are all SNP rs2454206 (I1762V). The clinical characteristics between patients with or without TET2 SNP, including sex, age, white count while diagnosis, chromosome abnormalities, death and relapse are not different between this 2 groups. Kaplan–Meier survival analysis is used to test the correlation between TET2 gene polymorphism to prognosis, including overall survival and event free survival. There was no difference.

Conclusion

As we know, we are the first group to publish TET2 gene alterations in childhood AML in Asian. We conclude the prevalence of TET2 mutations in pediatric AML patients is far lower than in adults and the TET2 polymorphisms are not associated with prognosis.
<table>
<thead>
<tr>
<th>Region</th>
<th>dbSNP rs# cluster id</th>
<th>cDNA position &amp; SNP allele</th>
<th>Amino acid position &amp; protein residue</th>
<th>Patient number</th>
</tr>
</thead>
<tbody>
<tr>
<td>intron</td>
<td>rs72224084</td>
<td>-/AGATAGAT</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>rs58201766</td>
<td>-/ATGATAGA</td>
<td></td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>rs59046770</td>
<td>-/TAGA</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>Exon 3</td>
<td>rs12498609</td>
<td>149 C→G</td>
<td>P29R</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>rs6843141</td>
<td>715 G→A</td>
<td>V218M</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>983 T→C</td>
<td>L307P</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1485 G→A</td>
<td>P474P</td>
<td>1</td>
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<td></td>
<td></td>
<td>1889 C→G</td>
<td>S609C</td>
<td>1</td>
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<td></td>
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<td>2667 T→G</td>
<td>F868L</td>
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<td>2503 C→T</td>
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<td>rs3796927</td>
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<td>3179 C→T</td>
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<td>Exon 9</td>
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</tr>
<tr>
<td>Exon 11</td>
<td></td>
<td>4601 A→G</td>
<td>E1513G</td>
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</tr>
<tr>
<td></td>
<td>rs2454206</td>
<td>5347 A→G</td>
<td>I1762V</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5502 A→G</td>
<td>Q1813Q</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5387 G→A</td>
<td>S1765N</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5657 C→G</td>
<td>A1865G</td>
<td>1</td>
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</tbody>
</table>
OFF-LABEL USE OF RECOMBINANT FACTOR VIIa IN PEDIATRIC PATIENTS: EXPERIENCE IN CHINA MEDICAL UNIVERSITY HOSPITAL

Te-Fu Weng, Ching-Tien Peng, Kang-Hsi Wu
Children's Hospital, China Medical University Taichung, Taiwan,

Introduction
Coagulopathy is an important cause of mortality in critically ill children. Traditional therapies to correct coagulopathy lead to great time delays and cause fluid overload in patients. Recombinant factor VIIa (rFVIIa) was found to be effective at controlling severe hemorrhagic symptoms of different etiologies in children without congenital hemorrhagic disorder. We reported our experience about off-label use of rFVIIa in pediatric patients with life-threatening bleeding.

Methods
Six patients with life-threatening bleeding and ages ranging from 0 to 13 years were recorded from 2008 to 2010 in China Medical University Hospital. Two patients were diagnosed with liver tumor, two patients with mediastinal tumor, one patient with immune thrombocytopenia and one patient with acute myeloid leukemia relapsed after cord blood transplantation. Life-threatening bleeding occurred due to surgical hepatectomy, bilateral herniarrhaphy, extracorporeal membrane oxygenation (ECMO) complicated and hemorrhagic cystitis. Lack of success to control bleeding by conventional methods was the cause to start rFVIIa. Median dose of rFVIIa was 127.6mcg/kg, ranging from 90 to 240mcg/kg each administration. All of the patients were given fresh frozen plasma and if necessary platelet transfusion before administration of rFVIIa.

Results
Bleeding was stopped completely in three patients after rFVIIa administration. Two patients with surgical hepatectomy and one patient with immune thrombocytopenia complicated hypovolemic shock after herniarrhaphy that all achieved hemostasis rapidly after rFVIIa administration. However, the effect of hemostasis was not achieved in two patients under ECMO support and one patient with late type of hemorrhagic cystitis after cord blood transplantation. No thrombotic complication was observed.

Conclusion
The off-label use of rFVIIa in critical pediatric patients is increasing rapidly despite the absence of adequate clinical trials demonstrating safety and efficacy. In our experience, for acute life-threatening bleeding, simultaneous administration of rFVIIa after failure of conventional treatment may contribute benefits to patient with ITP or after hepatectomy, but not to patients with ECMO or severe hemorrhagic cystitis.
SPONTANEOUS INTRAMURAL HEMORRHAGE IN HAEMOPHILIA
T.F. Weng¹, K.H. Wu¹, C.T. Peng¹,², M.C. Shen³,⁴

1. Children’s Hospital, China Medical University & Hospital, Taichung, Taiwan,
2. Department of Biotechnology and Bioinformatics, Asia University
3. National Taiwan University Hospital
4. Changhua Christian Hospital

Aim

The gastrointestinal hemorrhage is fourth common event in hemophilia. The incidence is varying, from 10 to 25%, and causes 4% of mortality. Spontaneous intramural intestinal hematoma (SIMIH) is a rare clinical condition that may result in potentially serious complications. The correct diagnosis early is imperative to avoid unnecessarily exploratory surgery. This study is aim to highlight this disease.

Methods

The medical records of the patients with SIMIH were retrospectively reviewed. Five patients were included in this study. Total 36 cases of SIMIH in previous lecture among hemophilia patients are also reviewed here.

Results

The most common symptom is abdominal pain (100%) and bleeding site of SIMIH is small intestine (52%). Abdominal computed tomography scan was diagnostic in all of our patients. The uncommon pre-contrast high density of bowel wall is characteristic sign of SIMIH. Most patients were followed up with conservative therapy and outcomes were very well.

Conclusion

The SIMIH is rare complication and must be kept in mind when hemophiliac patients have acute abdomen. Early diagnosis of SIMIH is proved by sonographic or radiological evaluation and conservative treatment always provide well outcome.

LUPUS ANTICOAGULANT AND ANGICARDIOLIPIN ANTIBODIES IN POLYTRANSFUSE BETA THALASSEMIA MAJOR
Weng Te-Fu¹, Wu Kang-His¹, Peng Ching-Tien¹, Shen Ming-Ching³

1. Children's Hospital, China Medical University & Hospital, Taichung, Taiwan,
2. Changhua Christian Hospital, Changhua, Taiwan

Background

The presence of anti-phospholipid antibodies (lupus anticoagulant, LA and anti-cardiolipin antibody, ACA) has recently been reported in polytransfused patients of beta thalassemia. Moreover, high prevalence of hepatitis C virus (HCV) infection and thrombotic risk is described in thalassemia.
Aims
We aimed at investigating the prevalence of ACA, LA, and their relation with HCV infection in patients with thalassemia major.

Methods
Presence of anti-HCV antibody, IgG ACA, IgM ACA and LA activity was determined in 36 patients with thalassemia major (male/female: 17/19 aged 12-37 years) registered at China Medical University Hospital, Taiwan. Two patients had thromboembolic events.

Results
LA was seen in 25% (9/36) of cases. The number of transfusions but not age was slightly higher in LA positive patients as compared to LA negative patients, however the results were not statistically significant. Anti-HCV antibody was positive in 15 (41.6%), IgG ACA in 7 (19.4%), IgM ACA in 21 (63%), and LA activity in 9 (25%) patients. 71.5% of patients positive for IgM ACA had a low titer of ACA. Strong positive IgM ACA were detected in 16.6% (6/36) of patients but no statistically significant correlation was found with age, number of transfusions, and coagulation parameters. No statistically significant difference in the prevalence of LA or ACA was found between HCV-infected and non-infected patients.

Conclusion
A high prevalence of LA and ACA, also the majority in low titers, was detected in patients with polytransfused thalassemia major in Taiwan irrespective of previous history of blood transfusion and presence of HCV infection.

TAIWAN HEALTHCARE INSURANCE SYSTEM
Eric Wu
TianShing Trading Co., Taipei, Taiwan
Taiwan Pharmaceutical Marketing & Management Association, Taipei, Taiwan

Health Insurance for All
Over the past 16 years, the government has successfully provided universal and quality health care to the people of Taiwan at affordable costs. In recent years, the Bureau of National Health Insurance (BNHI) has focused on ensuring care for socially and economically disadvantaged people and steadily improving its administrative efficiency and service quality. Today, Taiwan's National Health Insurance (NHI) program is a model of a single payer Social insurance system and has earned praise internationally.

Providing Care for the Socially and Economically Disadvantaged
The BNHI was founded on the principle of marshaling the resources of the majority to ease the difficulties less fortunate people have in paying for health care. Those who cannot afford their premiums are eligible for assistance from the BNHI. To help them overcome financial hardship and safeguard their access to care, the BNHI offers a variety of programs, including premium subsidies, relief fund loans, sponsorship referrals, and installment payment plans. The BNHI has also promoted an integrated delivery system (IDS) plan
to improve services in remote mountainous areas and outlying islands. The program brings socially disadvantaged residents in those areas much needed medical services.

Commitment to Upgrading Care Quality

With the introduction of a global budgeting system, which sets annual spending caps on broad health care sectors, the BNHI must ensure that health care quality in Taiwan will not be compromised due to resource constraints. The BNHI has consistently worked together with medical institutions to provide quality care that often goes beyond the call of duty to satisfy the needs of the insured. This commitment is consistent with the BNHI’s evolution. When the program was first launched in 1995, our main goals were to improve patients' access to health care by easing their financial burdens. With time, the BNHI gradually adjusted its focus to emphasizing the quality of health care, as defined by three new objectives. The first was to expand patients’ knowledge by making information on health care quality and services accessible and transparent. The second was to pay greater attention to the quality of medical services delivered to disadvantaged groups in remote areas and provide equitable and appropriate care. The third was to put greater emphasis on patient safety and make health care more patient-oriented. These three goals have led to the adoption of several measures to upgrade quality and efficiency that have improved the health of Taiwan's people, as seen through a host of indicators. The number of patients receiving holistic treatment for chronic ailments such as asthma and diabetes has risen, as has the overall level of satisfaction with the health care system. Emergency care visits and readmission rates have gradually fallen and the rate of growth of the incidence of major diseases has slowed down.

Capturing International Attention

The NHI program’s success in providing universal coverage and convenient access to care at low premium rates while containing the growth of medical expenditures has impressed many foreign visitors. In 2011, about 400 visitors from all over the world visited the BNHI and learned about the achievements of the NHI program. Several officials from the BNHI were also invited to other countries to share our experiences and expertise in managing the program. This widespread interest from the international community reflects the growing prominence of Taiwan’s National Health Insurance program as a health care model for countries around the globe.

Commitment to Improvement

While taking pride in its many achievements, the BNHI is constantly seeking further improvement by embracing such fundamental principles as promoting social equity, increasing efficiency, enhancing the quality of care and forging a national consensus. The BNHI has drafted strategic goals and concrete measures that are expected to enhance health care functions at every level of the system and strengthen community care. The NHI program benefits all of the country’s people and is truly a matter of pride for Taiwan.
TRENDS IN CANCER INCIDENCE AT LIMA METROPOLITAN CANCER REGISTRY: 1968 – 2005

Payet, Eduardo; Perez, Patricia; Poquioma, Ebert

Lima Metropolitan Cancer Registry, Epidemiology and Statistics Departament
Instituto Nacional de Enfermedades Neoplásicas
Lima, Peru

Background

Population based Lima Metropolitan Cancer Registry, pioneer in Latin America, works since 1968, hosted by Instituto Nacional de Enfermedades Neoplásicas; its results have delineated the Control Cancer efforts in the last four decades for all country. Territory, coverage, and methodology are the same all this time, population age composition and size were changing: at early period, population covered by Cancer Registry was 2.8 million; and grow until 2005 with 8.4 million.

Methods

Age standardized rate (ASR) for cancer incidence: all cancers (excluding non-melanoma skin cancer) and select other cancer sites, were compared for several periods: 1968-1970, 1974-1975, 1978, 1990-1993, 1994-1997 and 2004-2005. Percent changes were calculated between de first and late period.

Results

ASR incidence for all cancer, both sexes, increased from 156.7 to 174.8 per 100,000; variations were seen for specific cancer sites: cervical cancer (56%), stomach cancer (both sexes) (23% female, 45% male) and lung cancer (male) (40%) decreased; breast cancer (41%), prostate (116%), colon (64% female, 64% male) and lung (female) (102%) increased. Changes have several grades: breast and prostate has a high rate increase; colon and lung cancer are increasing but slowly. Cervix uterine and stomach cancer (male) have a strong decreased, while lung and stomach cancer (female) have slow decrease.

Conclusion/discussion

Cancer Control at Peru has a rise its activities since 2002. Cancer figures and results from Lima Metropolitan Cancer Registry are useful for the Cancer Control program. The changes observed are possible because: more access to health services (early premalignant diagnosis and new diagnosis technology); changes in life styles, general salubrity, more information about prevention. Cancer Registry population based is the tool capable for monitoring these changes. Is necessary other population based cancer registries in more cities at Peru.
ACUTE MYELOID LEUKEMIA DISTRIBUTION IN KYRGYZSTAN

Asel A. Usenova
Department of oncology, radiology and therapy, Kyrgyz - Russian Slavic University, Kirgizstan

Epidemiology research of leukemia indicates undeniable connection with the influence of the incidence of certain factors external and internal environment. In this paper we examine the primary incidence acute myeloid leukemia in Kyrgyzstan, as well as the features of distribution according to age and sex of the patients.

Objectives
The purpose of this study is to investigate the prevalence of acute myeloid leukemia in Kyrgyzstan, according to age and sex characteristics.

Materials and methods
The research investigated the period from 1991 to 2010 (20 years) and used annual data on the population of the republic areas during the study period, calculated crude, age-specific and standardized on the world standard population incidence rates per 100 thousand populations.

Results
There were 570 cases of acute myeloid leukemia in Kyrgyzstan (1991-2010), of which 271 cases (47.5%) were women and 299 (52.5%) - male. The patients' ages ranged from 15 to 87 years, mean age was 41 ± 0.4. The most number of cases of acute myeloid leukemia registered in Bishkek, Chui and Osh regions, 24.9%, 24.6% and 21.2%, respectively.

The peak incidence rate of acute myeloid leukemia occurred in the age of 80-84 and 65-69 years, with an incidence of 2.7 and 2.07 per 100 000, respectively. Age-specific incidence rates over the age of 85 years and 15-19 years have the lowest value was 0.3 and 0.73 per 100 000, respectively.

In calculating the standardized incidence rate with the world standard population, the incidence was 0.71 per 100 000 of the world population. The standardized incidence rate considering the world standard population with acute myeloid leukemia in males had a higher value compared to women, making 0.70 and 0.60, respectively.

Age-specific incidence rates in women were the highest recorded in the age 65-69 and 80-84 years, with an incidence 1.87 and 1.84 per 100 000 population. Among men, the highest incidence rates are also highlighted in the age of 80-84 and 65-69 with the values of 3.50 and 1.91 per 100 000, respectively. The lowest values observed at the age of 15-19 years for women and 45-49 for men, with an incidence 0.49 and 0.72 per 100 000, respectively.

Thus, on the basis of the above, we arrived to the following conclusion, that the incidence of acute myeloid leukemia in Kyrgyzstan uneven and low standardized incidence rate was 0.71 per 100,000 populations.
RETROSPECTIVE ANALYSIS OF THE HEMOGRA MGS OF CHILDREN WITH ACUTE LYMPHABLASTIC LEUKEMIA
S.H. Danielyan1,3, L. R. Sargsyan1,3, L. R. Avetisyan2, I.Ch. Azizyan2, D.G. Zohrabyan1,3
1. Clinic of Chemotherapy of “Muratsan” Hospital Complex of Yerevan State Medical University
2. Clinico-diagnostic laboratory of “Muratsan” Hospital Complex of YSMU
3. Department of Oncology of YSMU
Yerevan, Armenia

Neutropenia is defined as a decreased number of functionally active neutrophils per unit of blood volume. Neutropenia is one of the most frequent complications of chemotherapy in blood cancers as a result of bone marrow stem cells proliferation inhibition. Neutropenia leads to the development of severe bacterial, fungal and viral complications. The amount of life-threatening infections developing after chemotherapy depends on the degree and duration of neutropenia.

During this study in the Clinco-diagnostic laboratory of “Muratsan” University Hospital examinations of WBC in peripheral blood of children with ALL were performed. Under our observations were 40 children with ALL treated and evaluated in the Clinic of chemotherapy of “Muratsan” Hospital from 2008 to 2012. All patients were managed by German BFM 2000 protocol consisting of 3 main parts: induction of remission; consolidation; re-induction, intensive chemotherapy with total duration approximately of 8 months & maintenance therapy for 1-2 years.

According to the results of the study in 40 studied patients mortality was 7, 5% (3 patients) at different stages from various complications; leukopenia with WBC count less than $1000 \times 10^9/L$ developed in 30% of patients at the beginning of induction, full aplasia with WBC count less than $500 \times 10^9/L$ developed in 52% of patients at the third week of treatment. In 70% of patients leukopenia lasted 5 weeks. 55% of patients developed leukopenia with WBC count less than $500 \times 10^9/L$ at the consolidation phase.

To date, one of the causes of death from chemotherapy is the development of septic complication and septic shock in the presence of neutropenia, therefore an appropriate treatment is essential for the restoring of the number of white blood cells.

ACTUALITY OF THE IDENTIFICATION OF TRANSFUSIONALLY DANGEROUS ANTIGENS IN ONCOLOGICAL AND HEMATOLOGICAL PATIENTS
I.Kh. Azizyan1, S.H. Danielyan1,3, L.R. Avetisyan1, L.A. Harutyunyan2,3, G.N. Tamamyan2,3
1. Clinico-diagnostic laboratory of “Muratsan” Hospital Complex of YSMU
2. Clinic of Chemotherapy of “Muratsan” Hospital Complex of Yerevan State Medical University
3. Department of Oncology of YSMU, Yerevan, Armenia
Patients with cancer receiving chemotherapy usually need blood component transfusion, but besides therapeutic effects it can lead to post-transfusion reactions and complications. Currently, in some clinics donor blood for recipient transfusion is chosen only taking into account compatibility according to the ABO antigens system, and Rh(D) of the Rh-Hr system. With this type of selection, repeated blood transfusions of blood components can cause hemolytic reactions, especially, because of so called «little antigens» - C,c, E,e of Rh-Hr system and K antigen of Kell system. Erythrocyte alloantigen sensibility occurred as a result of long term hemo-component therapy limits the choice possibility.

Taking into consideration all these facts, we analyzed the prevalence of basic transfusionally dangerous antigens A, B, C, D, K, c, C, E, e in recipients in the Clinic of Chemotherapy of “Muratsan” Hospital Complex of YSMU and healthy population. Dissemination of phenotypes of ABO, Rh-Hr and Kell systems were examined within the patients with different oncological and hematological diseases.

In total 40 patients were examined: 22 patients with different solid tumors, 10 with leukemia and 8 with lymphoma. 24 donors and military personnel, who passed the examination, formed the group of healthy contingent. All samples of blood donors and patients were studied for ABO, Rh-Hr and Kell, using monoclonal antibodies of European labels.

As it is obvious from the prevalence of antigens among the examining recipients, K antigen is not seen, and it stands after D antigen in the immunogenicity antigen scale.

But antigen E is not met within the examining group with leukemia. During the investigation of several patients chimerism of antigen was observed after transfusion.

Hence, it is relevant that the use of blood components of higher quality, together with optimal immune-hematological examination of donors and recipients, will allow to decrease the post-transfusion risk connected with erythrocytes allo-immunization, and will help to use the donor blood more rationally.

**Table 1.** Antigen distribution of ABO, RH-Hr and Kell showed the following results.

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Summary</th>
<th>The frequency of antigens (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>A</td>
</tr>
<tr>
<td>Solid tumors</td>
<td>22</td>
<td>11(50%)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>8</td>
<td>4(50%)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>10</td>
<td>6(75%)</td>
</tr>
<tr>
<td>Control group</td>
<td>24</td>
<td>13(54%)</td>
</tr>
</tbody>
</table>
DISORDERS OF GROWTH HORMONE IN CHILDHOOD

R.L. Markosyan

Department of Endocrinology of “Muratsan” Hospital Complex of Yerevan State Medical University, Yerevan, Armenia

Background

Growth is a fundamental physiologic process that characterizes childhood and is followed as an indicators of child’s health. One of the reasons of growth failure is growth hormone (GH) deficiency. The incidence of GH deficiency has been estimated as approximately 1 in 10000 in live-births.

The most pronounced clinical manifestation and most severe prognosis have patients with GH deficiency.

GH deficiency may be complete or partial. It may also be classified as isolated GH deficiency or combined pituitary hormone deficiencies (MPHD- multiple pituitary hormone deficiency); congenital or acquired; idiopathic or organic.

Clinical features of GH deficiency vary and depend on the age of onset and severity of GH deficiency, association with other pituitary hormone deficiency. Patients with GH deficiency should be treated with recombinant human GH (rhGH) as soon as possible after the diagnosis is made.

Aim of the study

To evaluate incidence of GH deficiency in children in Armenia

Methods

An isolated assessment of pituitary GH level has no any diagnostic value. Therefore measurement of GH reserve upon pharmacological stimuli has been suggested, and the diagnosis of GH deficiency is made based on this test results. Pharmacological stimuli have included clonidine, insulin and arginine. In a child with clinical criteria for GH deficiency a peak of GH concentration below 7 ng/ml has traditionally been used to support the GH total deficiency, and peak 7 - 10 ng/ml to support the GH partial deficiency.

Patients with GH deficiency should be treated with recombinant human GH (rhGH) as soon as possible after the diagnosis is made.

Results

Since 2008 until today we identified 22 patients with GH deficiency, with 90,9% being male and 0,1% female. According to the form of GH deficiency the patients are divided as following: 14 (63,6%) patients had isolated deficiency of GH; 8 (36,4%) had GH deficiency combined with other pituitary hormones’ deficiency. Among these 22 patients 14(63,6%) had GH total deficiency and 8 patients (36,4%) had GH partial deficiency.

Brain MRI investigations of cohort demonstrated that 50% had organic pathology of the brain:

- pituitary hypoplasia in 4 (18,2%) patients
- posterior ectopia and hypoplasia of the pituitary in 1 (4,5%) patients
- adenohypophysis hypoplasia associated with neurohypophysis agenesia in 2 (9,2%) patients
- brain tumors in 4 (18,2%) patients
Other 11 (50%) patients on brain MRI have not any changes.

Conclusion

Unfortunately, growth hormone medicines are not produced in Armenia, and we have not centralized purchases of them. Patients cannot afford to buy medicine due to high prices. In majority of the world countries treatment of growth hormone deficiency is carried out on behalf of the government of that country; however, it is not available for our patients.

Actual problem is determined also by prior diagnoses complications, poor data on hormone secretion, on hormone replacement treatment and badly explored results. It is of priority to estimate the features, anthropometrics, and clinical, hormonal, metabolic changes of various types of growth hormone deficiency, algorithms development for pediatrician to mark prior growth failure at childhood and differential diagnosis of various forms of growth hormone deficiency and timely correction at their revealing. : in Armenian medical literature there is no any data concerning growth hormone deficiency extent among Armenian population and essential step to the optimization of patients care will become the establishment of National Register for patients with growth hormone deficiency; this will allow to obtain objective information on disease extent.

Cooperation of the specialists with the Register will lead to the improvement of diagnosis methods related to growth hormone deficiency and increase the quality of medical assistance.

EFFECTS OF PROBIOTICS ON ANTIBIOTIC RESISTANCE OF COMMENSAL E. COLI ISOLATED FROM INTESTINAL MICROFLORA OF PERIODIC DISEASE PATIENTS

N.A. Harutyunyan, A.M. Manvelyan, S.S. Mirzabekyan, L.M Malkhasyan

Armenian National Agrarian University, Yerevan, Armenia

The research has been carried, and the spreading of antibiotic resistant E. coli isolates has been analyzed, taking into consideration the relevant study of periodic disease in the Republic of Armenia and the existence of different disbiotic malfunction in intestinal microflora of PD patients, before and after probiotic usage.

We analyzed the antibiotic resistant profiles of E. coli, isolates from the gut microflora of 45 FMF voluntary patients. None of the study participants has been treated with antibiotics or any other chemotherapeutic agents for at least 2-3 weeks before the investigation. The identification of investigated bacteria was done by Murray PR. E. coli isolates (at least 6 isolates from each person if carrying ones) from the faecal microflora of healthy voluntaries were tested to the next antibiotics in the following concentrations: tetracycline 15µg/ml, doxycycline 15µg/ml, amoxicillin 25µg/ml, chloramphenicol 30µg/ml, cefazolin 24 µg/ml and ciprinol 20 µg/ml. Statistical analysis was performed using the CHITEST (null hypothesis).

According to the analyses, the usage of probiotic Narine and Colibacteron decrease the spreading of
antibiotic resistance of gut commensal E. coli among the studied antibiotics.

The best result of getting the sensitive E. coli has been found after the patients’ usage of Colibacteron.

EVALUATION OF ANTIOXIDANT FUNCTION EXTRACTS OF WORMWOOD IN THE OXIDATION OF ERYTHROCYTE MEMBRANES
Sukiasyan A.R., Kirakosyan A.A.
State Engineering University of Armenia, Yerevan, Armenia

Oxidative damage to tissues has become a recurring them as a mechanism for the induction of variety of medical conditions including myocardial ischemia, cancer, inflammation, and aging. Erythrocyte membranes contain many polyunsaturated fatty acid moieties and they are susceptible to various oxidative stresses and are a target of such damage. Erythrocytes and their ghost membranes are oxidized by a free radical chain mechanism and the erythrocytes eventually undergo hemolysis. Natural antioxidants are extensively studies for their capacity to protect organisms and cell from damage induced by oxidative stress. Herbs are harmless sources for obtaining natural antioxidants. In this study we investigated the effect of Artemisia Absinthium L.’s extract on membrane damage and dysfunction of erythrocytes induced by hemolysis and lipid peroxidation. We developed novel approaches to correlate the level of lipid peroxidation and membrane damage for erythrocyte system. Our results shown that choose a method of extraction (time, temperature, using solution, etc.) can be determinate that pharmaceutical effect, which necessary for concrete case of organism damage. Our works out by mathematical computer program simulation for the determination of factors of stability membrane allow creating model kinetics of oxidation. This work was support by ANSEF Grant 05-NS-biochem-340

THE EPIDEMIC SURVEILLANCE OF HAEMOPHILUS INFLUENZAE TYPE B INFECTIONS IN YEREVAN
N. S. Melqonyan
Department of Epidemiology of Yerevan State Medical University, Yerevan, Armenia

In many countries of the world, where vaccinations against Haemophilus influenzae type B are not implemented, haemophilus infections represent significant issue for public health. Hib contamination can cause at least 3 million people have severe diseases and approximately 386000 death annually. The latter is more common in developing countries. The most common types of haemophilus infections are pneumonia, meningitis, epiglottiditis, septicemia that occur in children under 5 years of age, but the most vulnerable are 4-18 monthly infants. According to the literature
data, deaths emerged from meningitis caused by Hib constitute 3-40 % and 20% of severe bacterial pneumonia is caused by Hib bacteria. Antibiotic treatment develops bacteria stability that brings difficulties for Hib causal treatment. Nose-pharyngeal hib bacteriocarrier is found in non-vaccinated children up to 5 years.

Taking into consideration above mentioned problems, the only effective mean against Hib infections are immunizations. Combined vaccine (DTP/HB/Hib) was introduced to National Vaccination Calendar of the Republic of Armenia in September 1, 2009. Vaccinations are done in 3 dosages in 1.5, 2.5, 3.5 monthly infants and after November 1, 2012 due to the changes of the Calendar they are being done in 1.5, 3 and 4.5 monthly infants. It was revealed from the researches done in 4 polyclinics operating under the supervision of Yerevan center and Nork-Marash territorial center Hygienic Epidemiological Inspection, that the average rate of DTP/HB/Hib3 vaccination of children up to one year was 93% in 2010, 91% in 2011 and 90% in 2012. Relatively low coverage of children vaccination was due to reasonable and unreasonable extensions, the letter is prevailing. Post-vaccinal unfavorable cases have not been recorded among vaccinated children. All the cases were with the expected reactions.

Pneumonia due to Hib infections occur more frequently, but Hib epidemiological surveillance is being committed during meningitis based on bacterial meningitis cases of hospitalized children up to 5 years. It is due to the fact that laboratory diagnosis of meningitis is effective and Hib prevalence can be assessed more accurately. Case records, reports, researches, presentation of monthly reports are done. Meningitis due to Haemophilus influenzae has not been recorded during 2010-2012 in Yerevan Center and Norq-Marash territorial center Hygienic Epidemiological Inspection.

Based on the above, though there has been done enormous work in HIB infections epidemic surveillance system, for improvements we need to provide sufficient level of DTP/HB/Hib vaccinations coverage, particularly 95% and more.

THE EPIDEMIC SURVEILLANCE OF POLIOMYELITIS IN YEREVAN

H. S. Hovhannisyan, N. S. Melqonyan, M. S. Haxverdyān
Department of Epidemiology of Yerevan State Medical University, Yerevan, Armenia

In order to maintain poliomyelitis-free status in Armenia it is very important to improve epidemic surveillance system of poliomyelitis. The significant part of this system is the organization and implementation of immunizations against poliomyelitis. Yerevan Center and Nork-Marash territorial center Hygienic Epidemiological Inspection is making supervision of immunization as well as vaccinations against poliomyelitis in 4 polyclinics operating under their control. Surveillance includes children vaccination sufficient enrollment provision, accounting and reporting, vaccine control and medical contraindications conduct, registration and accounting of postvaccinal unfavorable cases, as well as
epidemiological research over the latter. Inspections are carried out by quarterly immunoprophylaxis monitorings. In 4 surveyed polyclinics the data showed that the coverage of children up to 1 year (11 months and 29 days) in three dosage vaccines against poliomyelitis constituted 96% in 2010, 93% in 2011 and 92% in 2012. The coverage of children up to 2 years (23 months and 29 days) against poliomyelitis the four dosage vaccines constituted 96% in 2010, 93% in 2011 and 88% in 2012. The coverage of children up to 7 years (6 years, 23 months and 29 days) against poliomyelitis the five dosage vaccines constituted 97% in 2010, 96% in 2011 and 90% in 2012. During vaccination postvaccinal unfavorable cases have not been recorded.

The second essential part in epidemic surveillance system of poliomyelitis is morbidity of acute flaccid paralysis. Detection of poliomyelitis and acute flaccid paralysis cases is done in active and passive forms. Active epidemic surveillance has been implemented since 2007. Monitoring in the form of weekly visits are done in polyclinics. Under the surveillance of Yerevan Center and Nork - Marash territorial center Hygienic Epidemiological Inspection acute flaccid paralysis is found in passive form (2 cases was recorded in 2009 and in 2011). Polyclinics represent weekly zero reports. Monitoring concerning of submission of timely and complete reports, calculation of standard indicators and data analysis is carried out.

In conclusion, there has been done huge work in epidemic surveillance system of poliomyelitis, also the detection of 2 cases of acute flaccid paralysis testify the vigilance of the system. Higher level of OPV3 vaccination coverage in children up to 1 year is seen in 2010, OPV3 vaccination coverage level is relatively lower in 2011 and in 2012, and the latter is associated with undue delay of vaccinations. For the improvement of the system it is necessary to continue the detection of acute flaccid paralysis cases and provide sufficient coverage level in OPV3 vaccination (95% and more).

**ROLE OF THE MEDICAL OMBUDSMAN IN THE MODERN MEDICINE**

Mary Katvalyan

Public Administration Academy of the Republic of Armenia, Yerevan, Armenia

From the times of Hippocrates until now the only purpose of the healthcare system has been to guarantee people’s constitutional right to health care. Although, personal experience and knowledge of development mechanisms of diseases is very important, it does not diminish the possibility of medical errors even after many years of work experience. William Osler once noted correctly- "Medicine is a science of uncertainty and an art or probability"

The doctor is called to serve everyone, save thousands of lives at the expense of their own health maintaining and enhancing people’s health. However, along with the difficulties of their own profession, doctors are forced to bear and overcome the shortcomings of the health system and social management. Difficult conditions in which doctors are often forced to work, often
increases the torture to which they are exposed during their professional duties and the public's distrust.

There are many factors affecting the provision of efficient treatment, among which we can distinguish medical defenseless and vulnerable state before law and society. Unprotected doctor is afraid of introducing new methods of global health achievements, avoiding possible complications that inevitably appear in the world's best hospitals. Unsettled state of "medical error" is quite a complicated problem, which is one of the biggest problems of health care system not only in the RA but also in many countries of the world. The problem is even more difficult in the absence of the medical law, when the regulation of medical error completely enters the field of criminal law. In the same conditions, the legislation does not provide doctors protection before the law, if the doctors were subjected to torture or damage during professional duties.

The solution of these problems requires the creation of a medical ombudsman. The Ombudsman's task is to protect the interests and rights all medical providers from injustices or abuses of discretion, from gross inefficiency, from unnecessary delay and complication in administration of state rules and regulations, and from inconsistency, unfairness, unresponsiveness, and prejudice in the individual's experience with state activities. The Ombudsman exists to receive, examine and channel the complaints and grievances of members of all health care providers, and to secure expeditious and impartial redress.

The creation of Medical ombudsman is not an end in itself. Medical ombudsman is a body that equally protects both the treatment receiver and Medical provider's interests and rights, allowing increasing the quality of care provided.

This institute is meant to solve the problem of the protection of human rights in the health care sector, the area, which ensures the continuity of life on our planet.

THE BASIC DIRECTIONS IN CANCER CONTROL FOR ARMENIA

A.Z.Alexanyan, S.V.Arakelyan

National Oncology Center, Yerevan, Armenia

The steady growth of cancer morbidity and mortality rates among Armenian population calls the attention for the establishment of cancer control strategy in the country. This idea arises from the recognition of the fact that in most of the cases cancer can be prevented, additionally, as cancer treatment can be curative rather than palliative, early diagnosis is essential. In developed countries the priority of cancer control is given to the research of risk factors affecting cancer as a way to infer possible trends and causes of carcinogenesis, while the advancements in early detection techniques and specific therapeutic interventions consequently are placed on the second and third places.

The aim of the current work is the identification of priority areas of cancer control for Armenia at the present stage of country development.
It is well known that the effectiveness and outcome of the treatment of cancer depends on the detection stage of the disease - the earlier it is detected and diagnosed, the better the results of its therapy and higher the chances of the patient to return to his/her former way of life. Furthermore, research has shown that the average 5-year survival of patients with I stage tumors is 95-98%, II stage: 50-70%, III stage: 15-45% and IV stage is approximately 0-8%.

The economic efficiency of therapeutic interventions in patients with various stages of malignancies is incomparable - the initial stages of treatment requires the use of one or two therapeutic interventions, while at the III-IV stages the whole spectrum of extremely expensive therapeutic modalities are used: advanced surgical procedures, radiation and chemotherapy. The economical benefit of therapeutic interventions in health care is equal to 2.2-3.2; it is approximately 1.54-1.82 in oncology (data are presented for patients of lung and cervical cancers of I-IV stages). Given the fact that in overall structure of cancer patients the percentage of patients being diagnosed at III-IV stages is tremendously high (more than 50%), the cost of treatment of the initial stages of the malignancies is considerably low (for more than 30%).

From the above depicted, it is obvious that in Armenia the main directions of cancer control should be focused on early detection of cancer and precancerous conditions. It must be noted that the overall cost of diagnostic procedures is not comparable to the cost of the therapeutic interventions implemented in cancer management and equals to approximately 2% of the latter one.

Therefore, the realities of the day dictate the need for strengthening of the divisions of primary and outpatient cancer care and enhancing the utilization of preventive services in Armenia. These could be attained rapidly by optimization of implementation of all the forms of diagnostic preventive services and screening tests which will lead to identification and diagnosis of a number of cancer, precancerous and non-cancer diseases in its turn.

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**PRIMARY DIFFUSE LARGE B-CELL NON-HODGKIN'S LYMPHOMA OF THE SPLEEN, ACCOMPANIED BY PLEURAL EFFUSION: A CASE REPORT**

Alikhanyan T.P., Yeghoyan M.A., Hovhannisyan A.M.

Department of Clinical Laboratory Diagnostics,
Yerevan State Medical University

Yerevan, Armenia

The spleen is involved in 30-40% of non-Hodgkin's lymphoma cases, and primary spleen lymphoma (PSL) is a rare primary neoplasm of the spleen. This report described a case of a 63-year-old female patient with dyspnoea and heart palpitations. She had also history of type 2 diabetes mellitus. Chest radiography revealed pleural effusion of the left thorax.

On physical examination superficial lymph nodes and liver weren’t palpable; the spleen was non-
tender and palpable about 8 cm below the costal margin.

The complete blood count test, renal and liver function tests and LDH test results were within reference ranges. EBV was positive, HIV was negative. Pleural effusion cytology demonstrated monomorphic large cells with moderate amount of basophilic cytoplasm. Cells have round to oval vesicular nuclei with fine chromatin, 2-4 peripherally located nucleoli. By immunohistochemistry of a corresponding cell block specimen, the cells were strongly positive for CD45, CD20 and CD79. Cells with anaplastic morphology were negative for CD30 EMA, CD5.

Microscopic examination of spleen specimen showed features consistent with diffuse large B-cell lymphoma.

FAMILY CASE OF BOTULISM
Asoyan A.V., Shmavonyan M.V., Zardaryan E.A., Atoyan S.A.

Department of Infectious diseases, Yerevan State Medical University; Department of adults, “Nork” ICH
Yerevan, Armenia

Botulism is naturally occurring disease that can also be caused by accidental or deliberate exposure to botulinum toxins. Clostridium botulinum (C. botulinum) is a gram stain positive anaerobic organism and forms spores that can be found in soil, dust and aquatic sediments. Under suitable conditions, serologically distinct neurotoxins may be produced (A to G). Almost all human cases are caused by the A, B or E serotype. Almost all cases in Armenia cause of domestic prepared preserved food.

We find it noteworthy to introduce you a recent family case of botulism from Armenia.

Four members from the same family were referred in “Nork” Infectious Clinical Hospital in 01.02.2013 at the second day of illness, and the fifth member came to the hospital 2 days later.

There were mentioned using of the domestic prepared preserved vegetables (pepper, cucumber) in the anamnesis. The clinical course was stable for four patients with complaints to weakness, nausea, multiple vomiting, dysphagia, diplopia, dysphonia. After commonly accepted treatment with antitoxin ABE (A-10000 ME, B-5000 ME, E-10000 ME), desintoxication, antibacterial and symptomatic therapy, patients were discharged from the hospital at 12th day of the sickness in satisfactory condition, remaining under local medical observation.

Among the aforementioned cases there was an outstanding one we find it apt to mention, regarding 54 years old male patient H.B., who was accepted at the “Nork” Infectious Clinical Hospital at the third day of his illness. Against a background of the continuous vomiting there was a worsening in the state with a paralytic ileus evolving, which was inducement to take a patient to the intensive care unit. After an essential therapy the patient was discharged from the hospital at the 16th day of the diseases in satisfactory condition.
EFFECTIVE TREATMENT OF IMMUNE THROMBOCYTOPENIA WITH MONOCLONAL ANTIBODIES (RITUXIMAB)

Narine Gyozalyan¹, Lilit Sargsyan²

1. Faculty of Pharmacy, Yerevan State Medical University
2. Clinic of Chemotherapy of “Muratsan” Hospital Complex of YSMU

Chronic idiopathic thrombocytopenic purpura (ITP) is one of the most common immune disorders of blood cells, and in the development of it autoantibodies, directed against platelet antigens, play the leading role. ITP could be often unresponsive to conventional treatment i.e. prednisone, intravenous immunoglobulins, etc. This review summarizes the usage of MABs (monoclonal antibody) in the treatment of chronic ITP.

A clinical case of a 7 year-old girl with ITP, who is being treated at Clinic of Chemotherapy, “Muratsan” University Hospital Complex, Yerevan, Armenia, is presented in the abstract. Because of the long standing history of the disease and also the ineffectiveness of previous treatments, it was decided to include Rituximab into the treatment regimen (dosing: 375 mg/m² once per 3 weeks for (4 time). This led to long-standing remission.

Rituximab is one of the first drugs designed for target therapy and has high potential in the treatment of autoimmune diseases, including chronic thrombocytopenic purpura. So, more detailed studies of its pharmacokinetics and pharmacodynamics are necessary. Listed advantages of monoclonal antibodies require new, multicentral clinical trials, which will bring a new step in saving lives of patients and improving their quality of lives. It is not in vain that MABs are considered as “magic bullets!”

PALLIATIVE HOME CARE IMPLEMENTATION IN ARMENIA

Narine Movsisyan¹², Stephen R. Connor³⁴⁵, Lilit Mnatsakanyan⁶

1. Department of Intensive Care of Yerevan State Medical University, Yerevan, Armenia
2. Armenian Palliative Care Task Force, Yerevan, Armenia
3. Worldwide Palliative Care Alliance, London, UK
4. Open Society Foundations, New York, USA
5. UNICEF, New York, USA
6. Ministry of Health of Armenia

Introduction

The number of patients with cancer and other incurable life limiting diseases is progressively increasing worldwide, and Armenia is not an exception. Low cancer prevention and its poor early detection leads to a significant increase in the number of patients with incurable forms of cancer at the last stages. Usually, active treatment of these patients becomes ineffective and impractical. Discharged from the hospital to nowhere, these patients die slowly and painfully in the face of helpless relatives, unable to ease the suffering of their loved ones. In many countries, palliative care...
comes to help such patients, by improving the quality of life of patients, controlling and eliminating the painful symptoms that make life of these patients unbearable. The suffering patients and their relatives (caregivers) are the object of the palliative care. There are different types of palliative care (home care, outpatient, hospital care, inpatient and day care, and hospice care). Home care is the preferable form of care, as patients are served in a comfortable home atmosphere.

Palliative home care is currently the most acceptable and available form of palliative care yet. In Armenia the Palliative care project was implemented by the “Patients’ Rights Protection Center” NGO with four co-partners - National Oncology Center after A. Fanarjyan (Yerevan), Yerevan Muratsan Medical Center, Ararat Medical Center and Vanadzor number 1 hospital since 2011. The financial partner of the program is the Global Fund.

Methodology

The evaluation of patients’ condition was done using standardized questionnaires (the VAS pain scale, Hospital Anxiety and Depression Scale, Karnofsky Performance Status Scale, Neuropathic Pain Diagnostic Tool) and by face to face interviews. Further evaluation and follow up as done on the next and all subsequent visits to the patients. The team members also provided phone consultations to their patients. The main symptom patients were reported was pain, which was measured by the 0-10 Numeric Rating Scale, nociceptive and neuropathic pain were both measured. The most common non-pain symptoms were nausea, vomiting, cachexia, the disintegration of the tumor. Anxiety and depression also was measured by appropriate questionnaires.

During the year from July 2011 until June 2012 palliative care was provided to 132 patients (women 78 (59.1%), men 54(40.9%). The age range was from 17 years to more than 80 years old of the served population. The main contingent of patients covered by the pilot project suffer from cancer 103 patients (78.5 %), 28 (21.7 %) patients suffer from non-cancer diseases (diabetes mellitus, cardiovascular, neurological disorders, mucoviscidosis, ischemic stroke, COPD etc.) The average service length (mean) of these 78 patients is 64.06 calendar days, and median length of the service is 37 calendar days, the shortest term of service was 1 day and the longest service term was 228 days.

Conclusion

Four mobile teams provided home care and symptomatic treatment above mentioned symptoms. The lack of oral morphine has been a limiting factor in implementation of palliative care in Armenia. Injectable morphine, non-steroidal anti-inflammatory drugs, and some weak opioids are available but no oral immediate or slow release morphine or other strong opioids are available to date. Access to oral methadone was achieved very late in the 12-month pilot project period. A large volume of service was delivered. Many of these services are new to the health care system in Armenia and open a new dimension in how the sickest patients can be managed. Some reorganizing of the health care system resource utilization is needed to ensure that palliative care is given more priority to help advance health care reform and utilization.
VISCERAL LEISHMANIASIS
Asoyan A.V., Shmavonyan M.V., Atoyan S. A.

1. Department of Infectious diseases of
   Yerevan State Medical University
2. Children’s Department of “Nork” ICH
   Yerevan, Armenia

Visceral leishmaniasis (VL), also known as kala-azar, black fever and Dumdum fever, is the most severe form of leishmaniasis. Leishmaniasis is a transmissible diseases caused by protozoan parasites of the Leishmania genus. This disease is the second-largest parasitic killer in the world (after malaria), responsible for an estimated 500,000 infections each year worldwide. The parasite migrates to the internal organs such as liver, spleen (hence ‘visceral’), and bone marrow, and, if left untreated, will almost always result in the death of the host. Signs and symptoms include fever, weight loss, fatigue, anemia, and substantial swelling of the liver and spleen. Of particular concern, according to the World Health Organization (WHO), is the emerging problem of HIV/VL co-infection.

Leishmaniasis, especially visceral form was registered in Armenia in 1913. During the 20th century numerous cases were reported in 16 regions (at 700-1580m above sea level). Most of the cases are young children (under 5) and occur in areas bordering Afghanistan, Georgia, Iran and Turkey. Studies of over 4000 animals revealed that foxes and dogs are natural reservoirs.

Taking into consideration this infection worldwide spreading and being a serious problem regarding its high mortality, we find it apt to introduce one of the recent cases of visceral leishmaniasis from Armenia.

The male patient M.N. one year old was referred in the “Nork” Infectious Clinical Hospital with the preliminary diagnosis of visceral leishmaniasis from Kapan city, region of Syunik, Armenia. There were complaints to weakness, lowering appetite and weight loss, alternately rise in temperature and often repeating ARD (acute respiratory disease) during several months.

Objectively there were skin paleness, about 25% weight deficit, enlargement of liver and spleen.

After carefully examination of the patient there were discovered following results along with: pancytopenia (Hb-68.0, RBC-2.93x10⁶/µL, WBC-1.98x10³/µL, and PLT-40.0x10³/µL), normal level of liver-associated enzymes (ALT – 22 U/L, AST – 30 U/L). A thick and thin smear for malarial parasites was negative, Radiographic data included bronchitis, heart enlargement, thymus hyperplasia. Sonographic data included hepatosplenomegalgy. In marrow puncture amastigotes were directly visualized, confirming a diagnosis of visceral leishmaniasis.

The patient received Glucantim (meglumine antimoniate, Sanofi) according to the scheme (dosage by weight and age) without any significant drug toxicity. The patient became afebrile, and laboratory studies demonstrated normalization of his liver-associated enzymes and improvement in his leukopenia and anemia at the 7th day of treatment. The patient was discharged from the hospital at the 15th day of treatment and returned home, remaining under local medical observation.
INVESTIGATION OF REPRODUCTIVE RISK FACTORS FOR ENDOMETRIAL CANCER DEVELOPMENT AMONG WOMEN AGED 45-75 YEARS IN YEREVAN, ARMENIA: A CASE-CONTROL STUDY, 2007

S. Arakelyan, L. Abrahamyan, L. Poghosyan
American University of Armenia, Yerevan, Armenia

Introduction

Endometrial cancer (EC) is a hormone-dependent neoplasm that results in malignant transformation of the inner wall of uterus. It is one of the most common gynecologic cancers and accounts for 6% of all cancers in women, worldwide. Armenian women historically have lower risk of endometrial cancer compared to western countries. However, the incidence of endometrial cancer among Armenian women has substantially increased over the last 2 decades. Nowadays, endometrial cancer is a widespread malignancy among women in Armenia and is the second most frequent oncogynecological malignancy followed cervical cancer. According to the data obtained from Armenian National Oncology Center’s (NOC) Statistical department, in 1997, the incidence rate of endometrial cancer was 6.9 per 100,000 population, while in 2006, the incidence rate increased to 15.1. Meanwhile, if in 1997 the mortality rate from endometrial cancer was 3.6 per 100,000 population, in 2006 this number turned to be 7.3.

Objectives

The current study identified the reproductive risk factors of endometrial cancer among 45-75 years old women in Yerevan, Armenia and developed recommendations for early prevention of the disease.

Methods

The study utilized a case-control study design. Cases were patients aged 45-75 years with clinically and hystologically confirmed diagnosis of endometrial cancer who were registered at the National Oncology Center of Armenia from 2000 to 2006 (n=177). Controls were “healthy” women aged 45-75 years residing in Yerevan recruited through Random Digit Dialing (n=232). An interviewer-administered structured questionnaire was used during the telephone interviews with both cases and controls.

Results

Cases and controls were significantly different in several factors. According to the multiple logistic regression analyses, getting older than 55 years was associated with 2.5 times (OR=2.5, 95% CI 1.3-4.7) and 65 years with more than 9 times (OR=9.0, 95% CI 4.3-18.8) increased risk of endometrial cancer as compared to the younger age women (45-54 years). Older age at the onset of menarche (over 14 years old) was associated with threefold elevated risk of endometrial cancer. Gravidity was associated with a considerable risk reduction for endometrial cancer development (OR =0.1, 95% CI 0.03-0.38). Compared with normal weight women (BMI=19-24.9 kg/m²), obese women (BMI >30.0 kg/m²) had approximately 7.5 times higher risk of endometrial cancer. Oral contraceptive use and intrauterine device use was very low in this population while very high proportion of women...
experienced at least one induced abortion in their lifetime.

**Conclusion**

Older age, older age at the onset of menarche, obesity, and nulliparity were independent risk factors of endometrial cancer development. Based on the results it has been suggested to promote actively the concept of maternity and gravidity, healthy lifestyle and weight control, as well as family planning and particularly modern methods of contraception among Armenian female community.

**EVIDENCE - BASED MEDICINE**

Mary Katvalyan

Public Administration Academy of the Republic of Armenia, Yerevan, Armenia

In the RA, as well as in many developing countries of the world, the costs of medical assistance, as a rule, pay patients or their relatives, as the concept of "state order" has become highly uncertain since a long time ago. That is why many doctors are often reluctant to prescribe necessary and expensive investigations, taking into account that the patient would not be able to pay for the investigation. As a result, the patient does not undergo necessary investigation, thus, does not receive proper medical aid. Currently, when diseases have more complicated forms, it is very important to have clearly defined treatment schemes based on scientifically proven medical information. This idea was first discussed at the University of Toronto, and, now, it is widely used not only in Canada but also in all developed countries of Western Europe.

Evidence-based medicine is a medical practice in which the decisions on diagnostic, preventative and therapeutic interventions are made based on the evidence of their effectiveness and safety, which means- based on scientific evidence. As D. Cook stated, evidence-based medicine is a medical practice and, at the same time, is a form of learning, which allows in local healthcare systems to combine knowledge on pathological physiology and doctors’ experience of clinical research.

Evidence-based medicine is a technology of collecting medical information, analyzing, synthesizing and interpretation, which allows making scientifically proven decisions on diseases prevention, diagnosis, treatment and healthcare management.

It can be assumed that the introduction of evidence-based medicine will help to regulate pharmaceutical sphere. So, clearly defined treatment schemes will give the possibility for the government to define "Essential Drug List", thus regulating processes of licensing and avoiding importing and manufacturing questionable drugs. In this case prescription order also changes: the doctors will prescribe not the trade name of a drug, but the generic name. Thus, while buying medicine/drugs, people will not be guided in advance, in this case drug ingredients will be important, excluding doctor-pharmacy possible corruption channels. Equally important is the problem of postgraduate/further education. Currently, 1.5-2 months trainings for doctors are causing problems mostly in rural areas, while evidence based medicine continuous seminars with
the duration of 1-2 days will help to increase professionalism especially in rural areas. Turning to the problem of obtaining scientific information, it is necessary to note that the existing Republican Scientific Medical Library in Yerevan, in collaboration with the World Health Organization, in modern conditions of informational technologies provides all the opportunities to get necessary scientific information.

For healthcare system professionals it is very important to understand that evidence-based medicine is not a new way of conducting research but rather implementation of the results of scientific research in everyday medical practice; it is a tool, a means and condition to ensure quality and effectiveness of activities both in medical science and in clinical practice.
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