Abstracts for the 45th Annual Meeting of the AMERICAN SOCIETY OF HEMATOLOGY

RED CELL STRUCTURE/FUNCTION, METABOLISM, AND SURVIVAL, INCLUDING IRON

Abstract# 3711

Is Soluble Transferrin Receptor a Prognostic Cardiovascular Risk Factor? P. Lehmann*,[1] S. Braun*,[2] (Intr. by James Cook) *[1]Centralized Diagnostics Clinical Trials, Roche Diagnostics GmbH, Mannheim, Germany; [2]Deutsches Herzzentrum Muenchen, Klinik an der Technischen Universitaet Muenchen, Munich, Germany.*

In a case-control study with 678 patients and 229 controls the patients with CAD had significantly higher values of soluble Transferrin Receptor (sTfR). There was also a correlation between sTfR and the severity of CAD. In multivariate analysis, the sTfR was the strongest independent predictor of CAD. sTfR was found to be a sensitive tool for prelatent iron deficiency and for disturbance of iron utilization in Anemias of Chronic Diseases (ACD). We hypothesized that assessment of sTfR would enable to stratify risk among patients with ACD. Materials and Methods: We investigated patients with renal insufficiency, with Rheumatoid Arthritis, with Diabetes, with Chronic Inflammations, a healthy reference population and healthy seniors. The studies were carried out using Tina-quant® [a] Ferritin and Tina-quant® [a] sTfR assays, COBAS INTEGRA® sTfR assay and Elecsys® Ferritin. Results: We found for sTfR (mg/L) the following values (Patients with Ferritin values < 100 µg/L were excluded.):

		sTfR [mg/L]				
Patients	n	Median	2.5th Perc.	25th Perc.	75th Perc.	97.5th Perc.
Renal Insufficiency	244	3.53	1.61	2.66	4.54	6.55
Rheumatoid Arthritis	97	4.48	2.26	3.51	6.23	11.75
Diabetes	107	3.40	1.79	2.68	4.21	6.03
Chronic Inflammations	457	2.92	1.62	2.40	3.53	5.53
Healthy Reference Population	164	3.29	2.01	2.69	3.98	6.69
Healthy Seniors	173	3.17	2.15	2.80	3.63	5.24

Patients with chronic diseases (RA, renal insufficiency, CAD, Diabetes) have significantly higher values of sTfR. The role of sTfR in iron deficiency seems to be clear. Little is known about the utility of sTfR in the functional iron deficiency. sTfR in interaction with Erythropoietin may act as a sensor of the intracapillary oxygen content. However, the fact that functional Iron deficiency tend to elevate sTfR levels may suggest that ACD, inflammation or metabolic derangement may represent different aspects of the same process and thus sTfR could be an early predictor of risk among patients with coronary syndromes.

Abstract# 3712

Co-Existence of Congenital Red Cell Pyruvate Kinase and Band 3 Deficiency. Rosa Branca*,[1] Elísio Costa*,[1] Susana Rocha*,[2,3] Henrique Coelho*,[1] Alexandre Quintanilha*,[2,3] José M. Cabeda*,[4] Alice Santos-Silva*,[2,3] José Barbot*,[1] (Intr. by Manuela M. Ribeiro) *[1]Serviço de Hematologia, Hospital de Crianças Maria Pia, Porto, Portugal; [2]Serviço de Bioquímica, Faculdade de Farmácia, Universidade do Porto, Porto, Portugal; [3]Instituto de Biologia Molecular e Celular, Universidade do Porto, Porto, Portugal; [4]Unidade de Biologia Molecular, Hospital Geral de Santo António, Porto, Portugal.*

Co-existence of pyruvate-kinase deficiency (PKD) and erythrocyte membrane protein deficiency in the same patient has been rarely described.

The authors report the case of a 9-year-old Caucasian girl, born in northern Portugal, with chronic non-spherocytic haemolytic anaemia and without family history of anaemia. Basic haematologic studies showed anaemia (9.8 g/dL), reticulocytosis (398x10⁹/L), high levels of total and indirect bilirrubin (85 mmol/L and 80.5 mmol/L, respectively), slightly high lactate dehydrogenase level (463 IU/L) and undetectable haptoglobin levels. The blood smear revealed red cell anisocytosis and anisochromia with some elliptical and few tear drop shaped erythrocytes. Aethiologic study of this anaemia revealed PKD, due to two previously described mutations (426Arg→Trp and 510Arg→Gln). Since the blood smear revealed features not fully compatible with PKD diagnosis, additional tests were performed for the propositus and her parents, namely red blood cell membrane protein analysis. A decrease in proteins band 3 (15%) and 4.2 (18%) was found in the propositus. Her father presented only a decrease in band 3 (11%). Molecular analysis of the TATA-box region of the UDP-glucuronosyltransferase-1 gene revealed heterozygosity for a TA insertion [(TA)₆/(TA)₇].

In PK deficiency, genotype/phenotype correlation is difficult to establish. There is a great variability in the possible combinations of the mutant alleles, and, even in patients with the same known genotype (either in homozigosity or compound heterozigosity), a significant variability in phenotype is observed. Coinheritance of erythrocyte membrane protein defects could influence this observed variability. In our case, it is not possible to demonstrate the interference of the present membrane protein defect with the clinical picture shown by the patient. Nevertheless, we believe that a careful blood smear observation could lead to the identification of combined enzyme and membrane protein deficiencies. By doing so, it could be possible to better understand the variability of the phenotypic manifestations and the mutual interference of both deficiencies.

Abstract# 3713

Zinc Negative Modulation of Ferritin. Farid Haurani. *Cardeza Foundation for Hematologic Research, Thomas Jefferson University, Philadelphia, PA, USA.*

Indiscriminate intake of nutrients, vitamins and minerals could lead to side effects of varied severity. A case in point is zinc. Several side effects have been described to ingestion of zinc over a period of several months. Among the hematologic abnormalities are: poor absorption of copper leading to hypocupremia and anemia, poor absorption of iron, sideroblastic anemia (ring sideroblasts and cytoplasmic vacuolization), leukopenia and neutropenia. In this abstract four persons, two adult sisters, their mother, and an unrelated middle aged man, are presented. Three of the group were referred because of mild anemia associated with moderate but incommensurate weakness. One sister had a hemoglobin of 12.0 g/dl, the other 14.2, the mother 11.8 and the unrelated man 13.5. (Normal: (F) > 12.2, (M) > 14.5). Serum iron was normal 55-223 ug/dl (normal: 50-180 ug/dl),however, serum ferritin was low, 3.1- 16 ng/ml (normal > 20 ng/ml.). All took 50 to 100 mg of zinc/day for at least two years. Recommended daily allowance (RDA) is 15 mg and upper limit of 40 for patients with acne.

The man was studied further. One month after zinc was discontinued, his serum zinc level by atomic absorption was 145 ug/dl and a month later 86 (normal: 60-130). With the first serum zinc determination, other metals were tested; nickel zero, iron, copper and lead were normal. Bone marrow examination was normal but no iron. Iron absorption with radioactive iron was 28%, expected was >50%.. Oral therapy, 65 mg of elemental iron/day for three months increased serum ferritin meagerly (20-24 ng/ml, 4 determinations), and serum iron remained normal (85-150 ug/dl, 4 determinations). Intramuscular iron dextran raised serum ferritin to normal levels (75-160, ng/ml, 4 determinations) and serum iron remained normal (100 ug/dl). The mild anemia, probably unrelated to iron but to bone marrow failure as reported in the literature, became normal in the third month.

Rats, in pairs, were given zinc alone by injection (48 mg/ kilo, once or 0.48 mg/day x 10), with iron or alone in rats with inflammation. Sera were collected before and after. In the pair of rats which received zinc alone, serum ferritin fell from 1165 ng/ml to 40 and 211 to 32. When zinc was given to rats with inflammation, serum ferritin rose from 124 ng/ml to 572 and 13 to 645. Iron injected with zinc, also raised serum ferritin from 118 ng/ml to 270 in one animal and in another it became very high (4455).The pre-zinc specimen was lost (serum ferritin determinations of the rats were the courtesy of Dr. Gary Brittenham).

In conclusion, zinc over weeks or months in dosage greater than the RDA produces mild anemia and weakness. It produces hypoferritinemia probably in a shorter period of time and malabsorption of iron. However, recovery is slow. The studies performed in the patient and rats suggest that zinc induced hypoferritanemia resulted from failure of production since iron or inflammation could overcome the zinc effect. High zinc intake might be more serious in patients with iron storage diseases. However, in these patients interference with iron absorption may be on the positive side.

Abstract# 3714

Prevalence of HFE Mutations in a Multiethnic Population of California Newborns. Carolyn Hoppe,[1] Robert Watson*,[2] Christopher Long*,[2] Fred Lorey*,[3] Lara Robles*,[1] William Klitz*,[1] Lori Styles,[1] Elliott Vichinsky.[1] *[1]Hematology/Oncology, Children's Hospital and Research Center at Oakland, Oakland, CA, USA; [2]Program in Core Research, Roche Molecular Systems, Inc., Alameda, CA, USA; [3]Genetic Disease Branch, California Department of Health Services, Richmond, CA, USA.*

Background

Hereditary hemochromatosis is the most prevalent genetic disease in populations of northern European descent, occurring in approximately 5/1000 individuals. However, the prevalence of the common HFE mutations, C282Y and H63D, has not been confirmed in a large, unselected, multiethnic population.