Moebius Strip Like Pathology: Mechanisms, Diagnosis, Treatment Correction

S. Kulishov[1], O. Iakovenko[2]

[1] Internal medicine No 1, HMEIU "UMSA", Poltava, Ukraine; [2] Daily permanent establishment, V.P. Komissarenko Institute of Endocrinology and Metabolism AMS Ukraine Kyiv, Ukraine

Abstract *Proposed and tested an algorithm for diagnosis of Moebius strip like pathology, as prerequisite for treatment correction. The algorithm is reduced to initialization of study objects as a Moebius strip, in particular symptoms, syndromes, diseases, multimorbid states; clarification of investigation objects as non-orientable two-dimensional surface; cutting a Moebius strip like clinical data, variability to form two disjoint Moebius strips; clarification of chirality Moebius strip turn; the determination of Moebius strip like constituents as the object of research and their 3D representation; clarification of Moebius strips turn chiralities of constituents; the adoption of diagnostic and therapeutic solutions based on geometry of the pathogenetic and sanogenetic mechanisms. Thus, our algorithm may be basis for making diagnosis and treatment decision.*

Keywords*: Moebius strip like pathology, diagnosis*

1. Prerequisites of the application of Moebius strip like pathology mechanisms

It's known the Moebius strip like space orientation of depolarization processes were characterized by the change of supraventricular pacemaker on ventricular and inverse [1]. Moebius strip like arrhythmias in the patients with sinus node dysfunction were displayed as a combination of supraventricular and ventricular extrasystoles, fibrillation and flutter transformation from atria to ventricles [1].

The patients with complete atrioventricular block had the Moebius strip like changes of depolarization / repolarization geometry, as the alternation of proximal and distal ventricular rhythms [1].

The specifics of the geometry of depolarization and repolarization processes in the patients with full atrioventricular block or binodal syndrome may be considered in elaborating differential treatment programs to be used in microcomputers for implantable cardiac pacemakers [1].

Analysis of the cardiac depolarization / repolarization geometry may serve as additional criteria for sudden death prognosis [1].

Anxiety and depression can be a manifestation similar to the Moebius strip [2]. When comorbidity prevalence is over 50%, doubts about the validity of the diagnosis may be raised [2]. If comorbidity is so common, does this reflect a weakness of the diagnosis [2]?

Does it mean that the comorbidity itself should be a diagnosis? Or do the comorbid conditions reflect one underlying entity, with common etiology, expressed in two different phenotypes [2]? This might be the case with anxiety and depression. Actually, they are so clearly linked that the relationship resembles to many a Moebius strip [2]. Like in the Moebius strip, when looking at it, it is impossible to say where one edge ends and another begins [2].

Cutting along the middle of a Moebius strip makes a similar construct, more twisted, but larger and more easily examined and described [2]. Cutting along the middle of the new, larger shape results in two separate loops; each more twisted, and very closely intertwined, but nevertheless two distinct entities [2].

It remains to be seen whether continued research will reveal comorbid anxiety and depression to be two intertwined disorders or a single pathology with two different phenotypes [2].

The hope is that using various underlying endophenotypical tools will assist in unraveling the nature of the anxiety-depression [2].

Does depression exist without anxiety [3]? The affective dysregulation characterizing the comorbidity between anxiety and depression in a range of clinical populations is typical manifestation [3].

Anxiety is an integral and essential part of depression [4]. Moreover, anxiety symptoms should be considered a significant predictor of depression severity and the level of a patient's functional recovery, and can be utilized in choosing a treatment intervention [4].

Depression and anxiety disorders share a significant nonspecific component that encompasses general affective distress and other common symptoms [5]. General distress, physiological tension, and hyperarousal are more specific to anxiety, and melancholia and pervasive anhedonia are more specific to depression [5].

The purpose of this investigation was to determine Moebius strip like pathology as basis for making diagnosis and treatment decision.

2. The methodology of determination Moebius strip like pathology for making diagnosis and treatment decisions

Algorithm for diagnosis of Moebius strip like pathology, as prerequisite for treatment correction, is reduced to:

- Initialization of study objects as a Moebius strip like, in particular symptoms, syndromes, diseases, multimorbid states;
- Clarification of investigation clincical objects, variabilities as non-orientable two-dimensional surface, that are embedded in three-dimensional Euclidean space;
- Cutting a Moebius strip like objects of research in the middle to form two disjoint Moebius strips;
- Clarification of chirality Moebius strip turn;
- The determination of Moebius strip like constituents (symptoms, syndromes, diseases, multimorbid states) as the object of research and their 3D representation;
- Clarification of Moebius strips turn chiralities of constituents;
- The adoption of diagnostic and therapeutic solutions based on geometry of the pathogenetic and sanogenetic mechanisms

Anxiety and depression [2], pro-ischemic and anti-ischemic, reperfusion and anti-reperfusion, stress and anti-stress, hypoxic and antihypoxic, pro-oxidant and antioxidant, inflammatory and anti-inflammatory, dyslipidemic and anti-dyslipidemic, pro-arrhythmic and anti-arrhythmic, destructive and anti-destructive processes can be manifestations similar to the Moebius strip. When comorbidity, co-processes are over 50% prevalence, doubts about the validity of the diagnosis may be raised [2]. The comorbid conditions, co-processes may reflect same underlying entities, with common etiology, expressed in two or more different phenotypes [2]. Actually, they are so clearly linked that the relationship resembles to many a Moebius strip [2]. Like in the Moebius strip, when looking at it, it is impossible to say where one edge ends and another begins [2].

3. Implementation of Moebius strip like pathology making diagnosis and treatment decision

An example of Moebius strip like low-intensity inflammation syndrome diagnosis in the patients with coronary heart disease, arterial hypertension is presented lower. It is known that the leading role in the pathogenesis of coronary heart disease, hypertension belongs to disbalance between pro-inflammatory and anti-inflammatory cellular and plasma factors. Moebius strip like processing of inflammation [6,7,8,9,10,11] is represented as 2 variants:

1. Identification of multiple foci of pro-inflammatory factors' activation and the consumption of anti-inflammatory, leading to the widespread inflammatory, including autoimmune processes to chaperones;
2. Identification of multiple foci of anti-inflammatory factors' activation with the consumption of pro-inflammatory, leading to the widespread activity of anti-inflammatory interleukins and chaperones.

An example of diagnosis a composite plurality of pathological process as Moebius strip like in the patients with coronary heart disease may be by the next algorithm.

It is known that the basis of coronary artery disease are disorders of the coronary circulation, ischemia, reperfusion, low-intensity inflammation, dyslipidemia, pro-coagulation, stress, vascular and heart remodeling. Moebius strip like sequence of processing is represented as:

- Initialization of the composite symptoms, syndromes with geometry similar to Moebius strip, in particular that typical for pro-ischemic and anti-ischemic, reperfusion and anti-reperfusion, stress and anti-stress, hypoxic and antihypoxic, pro-oxidant and antioxidant, inflammatory and anti-inflammatory, dyslipidemic and anti-dyslipidemic, pro-arrhythmic and anti-arrhythmic, destructive and anti-destructive processes;
- Identification of Moebius strip chirality as a reflection of the predominance of pro-gradient or anti-gradient pathological changes;
- Clarification of Moebius strip constituents (symptoms, syndromes) as the object of research and its 3D representation. Temporal and spatial sequence of symptoms, syndromes reflects the pathogenetic and sanogenetic processes that allowed correcting treatment.

Our results of Moebius strip like pathology investigation were confirmed by determination of inflammation consumption of anti-inflammatory factors' syndrome as triggers of vascular pre-atherosclerotic remodeling in the patients with essential hypertension [6]. The purpose of this study was determination the dependence between inflammation syndrome and vascular pre-atherosclerotic remodeling in the patients with essential hypertension (EH) [6]. The study included 36 patients (43-58 years old; men – 25, women - 12) with EH II with hypertensive heart [6]. We measured the interleukins – 1 beta, 6, 8, 10, C-reactive protein, factor of tumor necrosis alpha by ELISA. Holter electrocardiography monitoring and daily blood pressure monitoring was used [6]. Duplex Doppler-Echographic scanning of peripheral and common carotid arteries with the investigation of thickening of intimae-media complex and diameter of blood vessels was performed in B-mode by device LOGIQ 400 (U.S.) [6]. Short list of research data is presented as: Med. – median; Q – Lower and Upper Quartiles. The level of CRP was increased in the patients with EH { Med. 0.06, Q (0,03-0,09)}, and patients with coronary heart disease in combination with EH {Med. 0.09, Q(0,02-0,13)}, in last somewhat more (Pmw = 0.035). The diagnostic criterions of consumption syndrome of pro-inflammatory and anti-inflammatory cytokines are characterized by the combination of cytokine imbalance and different levels of remodeling of common carotid and peripheral arteries and heart [6]. The first stage is characterized by the elevation of the level as pro-inflammatory (interleukin-1-beta - 50 pg/ml, interleukin-6 -

more than 5 pg/ml, interleukin-8 - more than 30 pg/ml, C-reactive protein - over 8.2 mg/l, tumor necrosis factor alpha - 50 pg / ml) so as anti-inflammatory cytokines (interleukin-10 - more than 70 pg/ml) with the minimal quantity of affected arteries, with following rise of pro-inflammatory and drop of anti-inflammatory cytokines (interleukin-10 - less than 3 pg/ml) and remodeling 3-4 arteries and more with thickening of intimae-media complex from 1 to 1,29 mm [6]. Decreasing of pro-inflammatory cytokines and interleukin-10 determine maximal quantities (more than 4) of arteries, progression of thickening of intimae-media complex at end stage [6]. Thus, we determined dependence between inflammation consumption syndrome and vascular pre-atherosclerotic remodeling in the patients with essential hypertension [6].

Our next investigation allowed to determine influence of inflammation consumption syndrome on myocardial electrical instability in the patients with chronic coronary heart disease and sinus node dysfunction [7]. The purpose of the study was determination the dependence between inflammation syndrome, geometry of depolarization of atria, ventricles and myocardial electrical instability in the patients with CHD [7]. The study included 36 patients (62,83± 1,49; 8,92 years old - M±SEM,SD; men – 27, women - 9) with chronic CHD, including 24 with stable angina pectoris (SAP), II-III functional class. Geometry of depolarization of atria, ventricles investigated in 26 patients with SAP II-IV functional with sick sinus node [7]. 36 healthy subjects (59,3±0,85; 11,22 years old; men – 24, women 12) consist control group [7]. We measured the interleukins – 1 beta, 6, 8, 10, C-reactive protein, factor of tumor necrosis alpha by ELISA [7]. Holter electrocardiography monitoring and daily blood pressure monitoring was used [7]. An increase of one or a combination of several pro-inflammatory (interleukin-1-beta - 50 pg/ml, interleukin-6 - more than 5 pg/ml, interleukin-8 - more than 30 pg/ml, C-reactive protein - over 8.2 mg/l, tumor necrosis factor alpha - 50 pg / ml) and decreased anti-inflammatory cytokines (interleukin-10 - less than 3 pg/ml) promotes atrial fibrillation and/ or group ventricular extrasystoles, or ventricular tachycardia in 21 patients from 36 (P<0,01 by criteria of sign) [7]. The Moebius like space orientation of depolarization processes were characterized by the change of supraventricular on ventricular pacemaker [7]. In 18 patients with sick sinus syndrome from 26 (P<0,01 by criteria of sign) were displayed Moebius strip like arrhythmias as a combination of supraventricular and ventricular extrasystoles; atrial fibrillation and group ventricular extrasystoles or ventricular tachycardia [7].

Ratio of pro-inflammatory and anti-inflammatory factors for acute coronary heart disease is mirror of Moebius strip like pathogenesis [8]. Our study included 27 patients (64,52±1,82;9,08 years old – y.o.) with ST segment elevation acute myocardial infarction (STEMI) and 25 (64,15±1,58; 8,23 y.o.) - with unstable angina pectoris (UAP) [8]. Research included investigation of cardiac biomarkers, interleukin-10 (IL-10), high sensitive C-reactive protein (hsCRP), auto-antibodies to chaperone 60 (anti-Hsp 60) [8]. Ratio on division of the level anti-Hsp 60 and hsCRP (anti-Hsp 60 / hsCRP) at patients with STEMI was significantly lower {15,91±4,43; 23,04 conventional units (c.u.); (6,80-25,03); 5,73; (2,73-21,64), Pmw=0,0001} than in healthy 348,02±107,55; 340,12; (104,71-591,32); 275,33; (58,34-583,00). Index ratio of hsCRP to IL-10 {(hsCRP / IL-10) 1,50 ± 0,35; 1,83 c.u.; (0,78-2,22); 0,35; (0,07-2, 43) Pmw=0,001}; index of dividing the product of anti-Hsp 60 and hsCRP on IL-10 (anti-Hsp 60 * hsCRP) / IL 10} at patients with STEMI was significantly higher 109,80 ± 31,48; 163,57 c.u.; (45,10-174,51); 32,17; (2,85-209,42), Pmw=0,001 compared with the control group [8]. In patients with UAP were dominant index ratio of IL-10 to the absolute phagocyte count (IL10/ absolute phagocyte count) (M±SEM;SD;95%CI: 2,82±0,27; 1,37; 2,26-3,39 c.u..), moderate this ratio at patients with uncomplicated STEMI (1,94±0,38;1,08;1,04-2,84 c.u.) and reduced - in complicated STEMI (1,59±0,26; 1,11; 1,05-2,13; PANOVA 1-2-3=0,006) [8]. A similar trend was typical for index ratio of hsCRP to the absolute phagocyte count (hsCRP / absolute phagocyte count) [8]. Thus, severe inflammatory and anti-inflammatory activities is characteristic feature for the patients with UAP [8]. Moderate inflammatory and autoimmune inflammatory activity with reduced anti-inflammatory potential was typical for patients with complicated STEMI [8].

An example of Moebius strip like atrial fibrillation treatment is presented lower. It is known that for the treatment of atrial fibrillation we use drugs that influence on sodium, potassium, calcium channels, beta-adrenergic receptors. Moebius strip like treatment effects may be in 2 variants:

1. The prevalence of antiarrhythmic effects - transformation atrial fibrillation to normal rhythm, normalizing quantity of heart rate;
2. Manifestations of pro-arrhythmic effects, transformation of atrial fibrillation to flutter.

4. Conclusions

Our algorithm for determination of pathology mechanisms like a Moebius strip may be basis for making diagnosis and treatment decision. Modeling of this algorithm on Dragon language [12] help us to understand these processes better (scheme).

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The scheme

Algorithm for diagnosis of pathology like a Moebius strip, as background for treatment correction