Conclusions: The results indicated that Th17/Treg ratio exists in rheumatic MVD. This imbalance may have a role in the ongoing low-grade systemic inflammation in patients with RHD, and Th17/Treg balance may be a promising therapeutic approach in RHD.

P3904 | BEDSIDE
Histological and immunohistochemical characteristics of pannus in prosthetic valves
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Purpose: Prosthetic valve dysfunction due to pannus formation is an infrequent but serious complication. In this study we aimed to evaluate the morphological and immunohistochemical characteristics of pannus formation in patients with prosthetic valves.
Methods: A study included 35 patients (F=71.4%, M=28.6%) who underwent redo valve surgery due to obstructive pannus overgrowth. Prosthetic valves were examined with 2 and 3-dimensional transesophageal and transthoracic echocardiography (TTE). In this study, the resected tissue samples were stained with Hema Toxolin Eosin (HE) and underwent immunohistochemical study which included the biomarkers, α-smooth muscle antigen (α-SMA), desmin, epithelial membran antigen (EMA), CD34 (endothelial cell marker), transforming growth factor beta (TGF-beta), vascular endothelial growth factor (VEGF), factor VIII and matrix metalloproteinase (MMP-2 and 9). Presence and absence of expression on target cells were noted as positive and negative, respectively.
Results: The mean age of the study group was 44. The average time elapsed until redo valve surgery was 125.59 months (24-276). Twenty-two patients had only mitral, 1 had only aortic, 9 patients had both mitral and aortic, 2 patients had mitral and tricuspid mechanical valve. One patient had mitral bioprosthesis. Twenty-eight patients with mitral, 3 patients with aortic, 2 patients with both aortic and mitral, 1 patient with mitral and tricuspid mechanical prosthesis and 1 patient with mitral bioprosthesis had pannus overgrowth. Pannus formation was localized at atrial side in 48.6%, ventricular side in 28.6%, both atrial and ventricular side in 20% of the patients. The biomarkers were measured as follows: α-SMA (100%), desmin (68.6%), EMA (62.9%), VEGF (42.9%), TGF-beta (51.4%), MMP-2 (48.6), CD 34 (94.3%) and F VIII (97.1%) were positive. MMP-9 was negative in all patients.
Conclusion: Pannus formation, which is an overgrowth of fibrous tissue, is a chronic inflammatory reaction. Mediators, CD 34, VEGF and TGF-beta, which provide migration of smooth muscle cell and extracellular matrix and MMPs 2, which degrades extracellular matrix in the remodelling process, all may play role in the mechanism of pannus formation as the elements of the chronic active process.

P3905 | BENCH
Pharmacological mechanisms involving serotonergic 5-HT2B receptors in drug-induced valvulopathy
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Purpose: Recently safety data emphasized the close link between chronic therapeutic use of serotonergic 5-HT2B receptors agonists and cardiac valve degeneration but the pharmacological mechanisms have not been clearly understood. Histopathological lesions show cell proliferation with extracellular matrix deposition that can drive to valvular leaflets stiffness, severe cardiac insufficiency and surgical valve replacement.
In this work, we evaluated the effects of chronic administration of norexfenuramine (NDF) a highly selective 5-HT2B receptors agonist, on mice mitral valve leaflets. Adult male 125± mice (aged 12 weeks) were randomly assigned in 10 different groups and underwent a subcutaneous micro-osmotic pump implantation delivering either NDF (1mg/kg/day) or vehicle (sterile water) for 4 weeks. Four groups were designed with wild-type mice: vehicle, NDF; NDF + rilanserin (2mg/kg/day); NDF + SB 206553 (1mg/kg/day) and two groups of each type of these knockout mice: 5-HT2A-/-; 5-HT2B-/-; 5-HT2A/2B-/- receiving either NDF or vehicle. Mice were monitored by regular body weight, food and water intake, blood pressure measurement and echocardiography. At the end of the experiment, urine and CD39 and CD73. The comparison between wild-type vehicle treated and NDF mice didn’t reveal any significant differences in terms of food or water intake, body weight, echo-cardiography parameters, beside of a slight blood pressure increase from 115±5 mmHg to 126±6 mmHg for NDF treated mice. We also pointed out a significant increase of urinary amounts of 5-HIAA (52.6±7.8 mg/mg/24h) and 4.53 mg/mg/24h. Histological analysis of the heart revealed significant increased mitral valve leaflets thickness (36±6 micrometer vs 60±6 micrometer) and cellularity in NDF group (20±% vs control). These histological lesions are prevented in part by a pharmacological co-treatment with rilanserin and SB 206553 but not in NDF transgenic 5-HT2A/-/- treated mice. However NDF induced mitral lesions were fully prevented in 5-HT2B/-/- and 5-HT2A/2B/-/- mice.
In conclusion, we demonstrate the crucial role of 5-HT2B receptors in NDF induced valvulopathy. Experiments are currently evaluating cellular and molecular mechanisms.

P3906 | BENCH
Adenosine receptors mRNA expression in human leucocytes of patients with valvular disease
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Purpose: Adenosine is a potent anti-inflammatory autacoid; extracellular adenosine metabolism is generally thought to result from the sequential dephosphorylation of extracellular ATP to AMP by action of ectonucleoside triphosphate diphosphohydrolase (CD39) followed by degradation to adenosine by ecto-5'-nucleotidase (CD73). The diverse cellular actions of adenosine are mediated by four different adenosine G-protein-coupled receptors (A1R, A2aR, A2bR and A3R). In animal models, an up-regulation of ARs can be observed in cardiac tissue of failing heart (HF).
Recently ARs mRNA expression has been assessed in human whole blood providing a useful tool to evaluate the expression of ARs in diseases characterized by a marked inflammatory component.
The aim of this study was to evaluate the possible changes of transcriptomic profile between normal subjects (N) and cases with valve disease (Vlv).
Methods: Total RNA was extracted from leucocytes of N (n=7) and of Vlv pts (n=6) using TRIzol® reagent. A2aR and A3R in human leucocytes of patients (pts) with valvular HF (Vlv) as compared to healthy subjects (C).
Results: In human whole blood of Vlv pts significantly higher levels of mRNA expression, for each receptors analyzed with respect to C were observed (A1R: C=1.97±0.72, Vlv pts=10.9±3.27, p<0.0098; A2aR: C=0.45±0.15, Vlv pts=3.19±0.48, p=0.0057; A2bR: C=4.30±0.16, Vlv pts=5.00±3.92, p=0.05; A3R: C=1.39±0.26, Vlv pts=2.90±0.71, p=0.04). Also CD39 and CD73 resulted upregulated in human leucocytes of Vlv pts with respect to C. Significant correlations (p<0.05) were observed between all ARs themself as well as with CD39 and CD73.
Conclusions: The present study highlights, for the first time, an increase of ARs mRNA expression in the peripheral circulating cells of Vlv pts. The increase of CD39 and CD73 transcript levels is suggestive of a protective CD39-CD73 dependent adenosine production in advanced HF pts. These findings suggest that components of adenosine metabolism and signalling are altered in adenosine production and signalling in HF patients. Thus HF may benefit from adenosine-based drugs therapy after confirmation by clinical trials.