



DUBROVNIK
CROATIA

12th

HHT
INTERNATIONAL
SCIENTIFIC CONFERENCE

Clinical summary

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European
Reference
Networks



VASCern, the European Network on Rare Multisystemic Vascular Diseases

- Improve patient care
- HHT Europe: Spreading knowledge by teaching, using synergies by sharing.



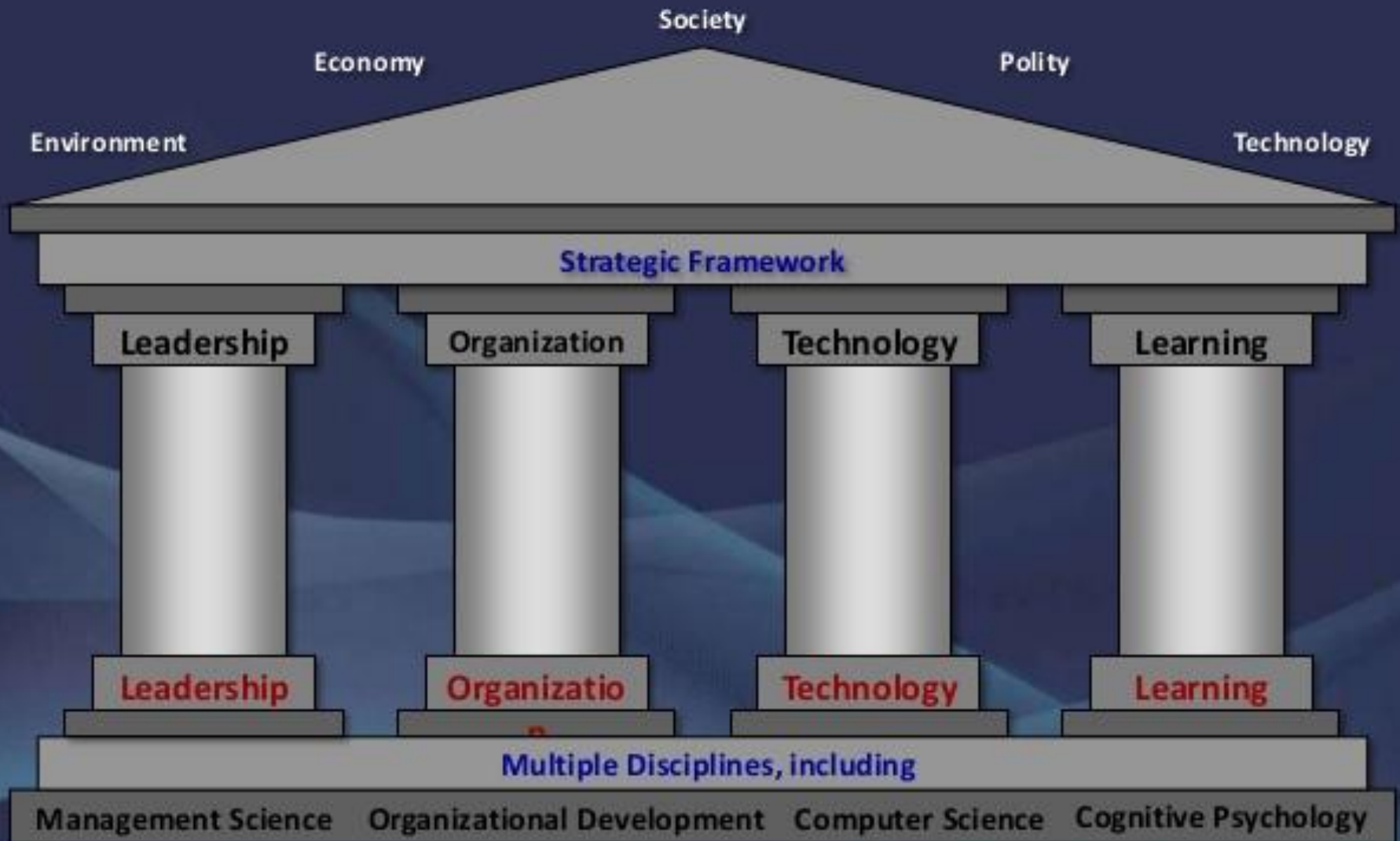
European
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Networks



VASCern, the European Network on Rare Multisystemic Vascular Diseases

- Improve patient care
- HHT Europe: Spreading knowledge by teaching, using synergies by sharing.
- Deliverables, including „pills of knowledge“

Pillars of Knowledge Management







Children and HHT

- Dutch group: it is safe to do screening with O₂-saturation and postpone TTCE to adult age
- Use of clinical criteria limited
- Screening for CVM in children differs
- In some children w PAVMs: surgery might be indicated



Bevacizumab

- Utah: B in 8 pts with high output heart failure and AVMs: right-heart catheter → 13% reduction of CI, ns; increase of pulm. a. p. in 2 pts
- Mayo: B for RBC tx-dependent pts and chronic nose and GI bleeds in 34 pts: effective, maintenance dose in most pts required
- Israel: does not seem to work for PAH but only for PH related to HVLMs/high cardiac output
- Dose increase might increase response rate



New drugs

- Endoglin antibody TR105 leads to a phenotype similar to HHT with epistaxis, telangiectases and anaemia but no visceral lesions; similar: Dalantercept (binds soluble BMP9) and PF03446962 (targets ALK1)
- Toronto: Pazopanib 50mg/day: very promising
- Gene therapy: might become available in the future; some obstacles: neutralizing AB, how to control expression
- Read-through drugs?
- Tacrolimus: upregulates ALK1



HVM

- Lyon: Ltx on 15 pts, clinics and QoL normalized, radiological recurrence in 8 with a delay of 12 ys (6-15), asymptomatic in all but one
- Lyon: Beva for 25 pts 8ys ago; follow-up:
2 no response, alive, no Ltx
5 complete response, 3 retreated
18 partial response, 2 Ltx, 1 waiting
- Can improve hepatic encephalopathy
- Might work better in diffuse disease
- Workshop: embolization is only an option in experienced hands; immune suppression after Ltx leads to kidney insufficiency in 20% after 10 ys;
Gossage: Ltx or try beva: give beva a try
- Bari: elevated γ -GT might be a predictor for AF



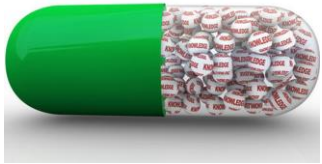
CVM

- A lot more data, but no clear recommendations, case-by-case decisions
- BVMCHHT: Radiosurgery: long-term obliteration after 5 years: 60% (similar to sporadic): good for multiple lesions, minimal complications, but latency time and lower rate of cure in comparison to surgery
- Embolization can be a very effective treatment in experienced hands



PAVMs

- New devices and method tested: MVP microvascular plug, gel coils, embolization of the sac
→ recanalization, children, costs, migration?
- Penn: graded TTCE might replace CT for post-treatment surveillance in pts with low grade shunt after treatment
- De-novo-rate: 0.7% per patient-year of follow up; remember also growth of small untreated PAVMs
- Screening and treatment increases life expectancy, it can even be normal
- SMAD4 can be associated with extensive PAVMs
- London: 13 of 24 pts with pavms showed silent cerebral ischemic changes on mri. Should pts with persisten pavms receive pharmacological stroke prevention?



PAVMs 2

- Systemic to pulmonary AVMs (SPAVM or thoracic vascular malformations)
drain into pulmonary arteries, no right-to-left shunt, TTCE can be negative, small percentage of pts; risk for hemoptysis and PAH
also other PAVMs can have systemic feeders
-



Epistaxis

- Utah: Vit D levels are associated with shorter epistaxis duration, confirms Paul Vase (1999)
- Bourdeaux: 40mg propranolol 2/day seems to work
- ALEGORI study confirms NOSE study: bevacizumab spray does not work
- Bevacizumab endonasally can lead to knee necrosis
- Denmark: Some patients have their onset of epistaxis after the age of 70



Inflammation / infection

- Innate immunity is affected due to decreased function of the macrophages
- Changes might be iron-related
- Endonasal manipulation might be responsible for some infections; genetic differences?



Other

- London: reminding the importance of using dietary iron and avoiding food high in salicylates
- Salamanca: Thrombus stabilization seems to be impaired
- Buenos Aires: high rate of overt GI bleeding
- Dutch: SMAD4 is associated with aortic dilation
→ control by imaging
- Utah: Mosaicism in non-blood tissue → hair bulb
- Promising reports from evolving centers in Croatia, South Africa and Japan
- More data on involvement of endoglin in arteriosclerotic disease



PX3 (Pentraxin 3)

- 109 pts, 16 ctrls
- seems to be the only lab value correlating with the severity of HHT and nosebleeds





Meir Mei-Zahav:
„Life is only temporary.“







THE PILLS OF KNOWLEDGE

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