

# Clinical research summary Part I

Tales of conferences past and present

Dr Claire Shovlin

## **Santander 27-31 May 2009**

**Excellent presentations**

**Large, statistically validated studies**  
**Insightful smaller studies**

**Stimulating open discussions**

**Welcoming atmosphere to the new attendees**

# Clinical Research Topics

**Diagnosis of HHT**

**Life expectancy in HHT**

**Quality of life in HHT**

**Management of organ involvement**

PAVMs

CAVMs

Spinal AVMs

*HAVMs (Jim Gossage)*

*Nosebleeds (Jim Gossage)*

**Management of specific periods of life**

children

pregnancy

dental work

**Processes**

**Antiangiogenic therapies** *(Jim Gossage)*

DVT

**Running an HHT service**

# Diagnosis of HHT

1) Are the Curaçao criteria still valid?



\*Shovlin, Guttmacher, Buscarini, Faughnan, Hyland, Westermann, Kjeldsen, Plauchu. Am J Med Genet 2000; 91; 66-7

# Diagnosis of HHT

1) Are the Curaçao criteria still valid?

Van Gent *et al* (Netherlands)

Compared clinical criteria to genetic test gold standard

N=910 (606 HHT1; 304 HHT2)

Univariate and multivariate analyses in HHT1 and HHT2

	Multivariate Odds ratios (95% CI)	
	HHT1	HHT2
Nosebleeds	20.3 (9.7-42.6) <i>p</i> <0.0001	11.3 (5.1-24.8) <i>p</i> <0.0001
Telangiectasia	16.9 (8.2, 34.7) <i>p</i> <0.0001	9.8 (4.2-22.6) <i>p</i> <0.0001
Visceral AVMs	39.0 (8.3, 183.5) <i>p</i> <0.0001	6.9 (0.8-63.4) <i>p</i> =0.09
Family history	<i>not testable</i>	<i>not testable</i>

⇒Validity confirmed

# Diagnosis of HHT

1) Are the Curaçao criteria still valid?

Bourgault Villada *et al* (France)

165 family members of HHT patients

Dermatologist (unaware of diagnosis) counted telangiectasia at different sites  
face, oral cavity, hands, fingers *and feet*

Diagnosed affected vs.unaffected status and compared groups

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	Age (years)				
	0-20	20-40	40-60	>60	
HHT	9	56	104	225	<i>all presented with</i>
Non HHT	2	4	9	29	<i>confidence intervals</i>

Suggested threshold for using telangiectasia should increase with age

# Diagnosis of HHT

## 2) New tools for diagnosis

Mohler *et al* (US)

**Finger transillumination in the dark**

**hand-held illuminometer**



**round dark lesions**

**Corresponded to sites of dilated arteries and veins by colour Doppler**

*Not seen in normals*

*(Not pathognomonic for HHT -also seen in Marfans, familial aortic aneurysm) ,*

# Life Expectancy in HHT

de Gussem *et al* (Netherlands)

Goodwin *et al* (Canada)

Life expectancy rather better than we thought, especially for men



de Gussem *et al* (Netherlands)

300 Questionnaires from HHT affected parents (574 sent out)

	mean age at death (range)		
	with HHT	without HHT	
males	70.4 (30-91.7)	72.1 (26.9-99.8)	$p=0.3$
females	70.5 (20.7-97.3)	77 (31.7-103)	$p<0.01$

# Life Expectancy in HHT

During pregnancy

Shovlin *et al* (UK)

Goodwin *et al* (Canada)

Shovlin *et al* (UK)

Life expectancy rather better than we thought



% of 484 HHT pregnancies

maternal (and fetal) deaths*	1.0 (0.1-1.9)
PAVM bleeds	1.4 (0.2-2.5)
Strokes	1.2 (0.3-2.2)
Spinal bleeds	0

\* All deaths occurred in women previously considered well.

In women experiencing a life-threatening event, prior awareness of HHT or PAVM diagnosis was associated with improved survival ( $p=0.041$ ).

# PAVMs

**Natural history** - migraine link  
- rupture during flight

*Van Gent et al (Netherlands)*

*Lacombe et al (France)*

**Screening issues (who/how) \***

**Devices used to treat**

**When not to treat** - Severe pulm. hypertension *Shovlin et al (UK)*

**Effects of treatment\***

**Follow up options** - MR scans

*Schneider et al (Germany)*

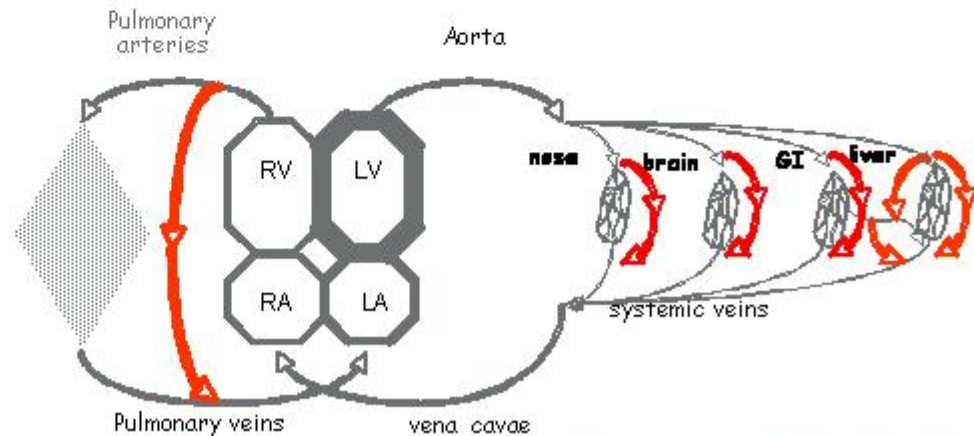
# PAVMs

**Systemic supply** - Lacombe *et al* (France)

Pre and post embolisation MDCT scans in 70 treated patients

Pre treatment systemic supply in 29%

Post treatment systemic supply in 38%



# PAVMs

## Screening issues

### 1) Children

- Fagnou *et al* (France)
- Shovlin *et al* (London)

### 2) Use of Contrast echo

- safety profile
  - grading systems
  - negative predictive value
- Gazzanigia *et al* (Italy)
  - Van Gent *et al* (Netherlands)
  - ~Blivet *et al* (France)

# CNS AVMs

Different phenotypes

- ter Brugge *et al* (Canada)

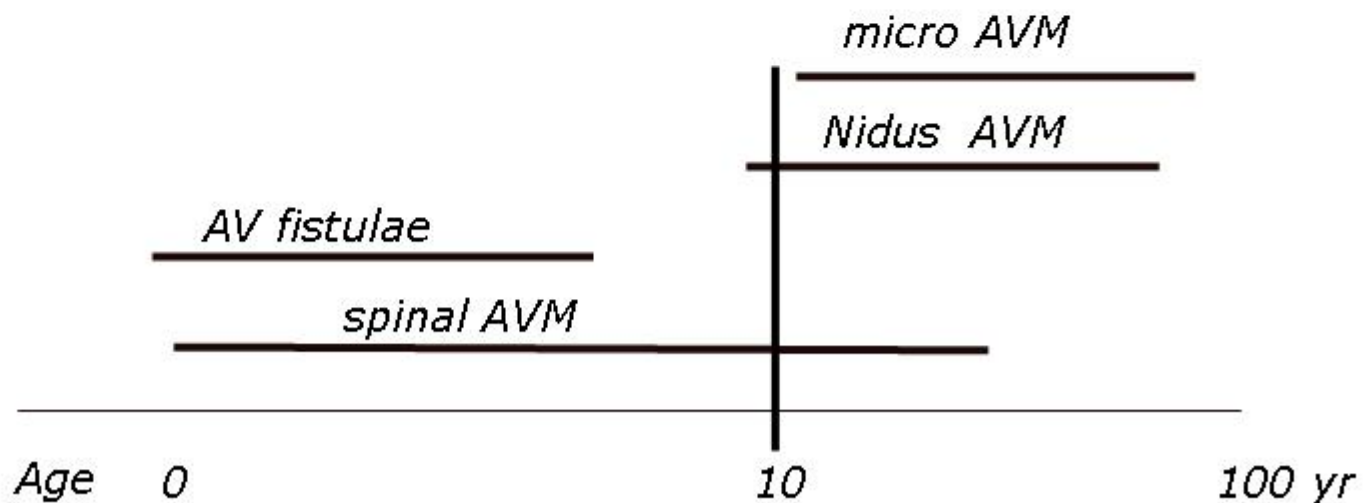
Phenotype-genotype

- Ozanne *et al* (Paris)

Age distribution

- Ozanne *et al* (Paris)

Ozanne *et al* (Paris)



# Deep venous thromboses in HHT

**Overall prevalence**                      Goodenberger *et al* (US)

**Management**                              Rivière *et al* (France)

## Goodenberger *et al* (US)

- 3.4% (13/346)

- experience of anticoagulating for up to 10 years

    INR target of 2.0

    No increased bleeds or transfusions (*selected group*)

## Rivière *et al* (France)

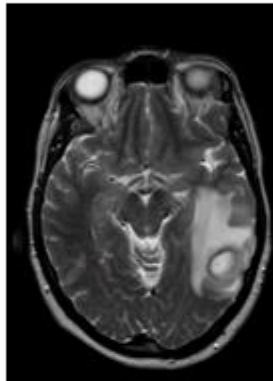
- 6% (50/ 830) patients from 3 French centres

- Risk factors: post partum; immobility; oestrogen therapy

- 32 patients tolerated anticoagulation

# Dental issues

Post AHA /NICE guidelines - [Shovlin, Bamford and Wray \(UK\)](#)



To prevent brain abscess

Pre 2007: Recommended PAVM patient use antibiotics before dental (and surgical) work

**AHA 2007 and NICE 2008 guidelines withdrew antibiotic recommendations for heart patients**

**Professor David Wray, Chairman of NICE Dental Committee**

PAVMs/HHT not considered by NICE /AHA

No evidence to change the status quo

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# Future directions

**Pooled data for key complication rates to assist in evaluating risk benefit analyses**

- successful treatment of severe pulmonary hypertension patients  
*stratified by PH type*
- stroke / abscess complications in asymptomatic children

**Statement regarding life expectancy in HHT**

**Standardisation of Echo methods**

- contrast injected
- grading



# 8<sup>th</sup> HHT

Hereditary  
Hemorrhagic  
Telangiectasia  
*Foucault - Osler - Weber*

## Scientific Conference

27-31 May 2009 | Santander, Spain

### Organizing Committee:

Roberto Zarrabéltia - Conference host  
Carmelo Bernabeu - Scientific chair  
Marianne Clancy  
Carlo Sabba  
Marie Faughnan  
Paul Oh  
Urban Geisthoff  
James Gossage

### Local Committee:

Alfonso Pérez de Molino  
Carmelo Morales  
Luisa M. Botella  
The HHT Spanish Unit

VENUE: **Magdalena Palace**  
REGISTRATION: [www.hht2009.com](http://www.hht2009.com)

Student fellowships and prizes to the best oral and poster presentations will be available.