

# Yale Centre models the way in the treatment of AVMs

The vast majority of people with Pulmonary Arteriovenous Malformations (PAVMs) suffer from the genetic disorder hereditary hemorrhagic telangiectasia (HHT) of which two forms have been identified, HHT 1 and HHT 2. At the moment the biological explanation of how these AVMs develop is not understood. However, HHT is a very common autosomal dominant disorder with experts suspecting it to be more prevalent than Marfan syndrome. Patients present with a variety of clinical problems determined by the organ(s) involved, with the condition occurring across the globe and not limiting itself to people of any race, ethnic or national group. As Dr. Robert White of the internationally renowned clinic, the Vascular Malfunction Center at Yale University, says, "This is a critical point which is not yet understood in Asia. In Asia, of course as expected, genetics is not a hot topic and culturally "taboo". We are working on this but have treated and seen Chinese, Japanese and Thai patients with HHT and no diagnosis." This disease, which has no national boundaries and which may be a cause of AVMs in the brain and liver as well as the lung, has meant that those who treat the condition have come, through necessity, from many medical disciplines and from around the world.

Dr. White and the Vascular

Malfunction Center ([www.hhtavm.org](http://www.hhtavm.org)) have been treating AVM patients, and training other centres to do the same, for many years. Dr. White developed the technique of pulmonary arteriovenous malformation (PAVM) embolization in 1978 with Dr. Peter Terry at Johns Hopkins Hospital, reporting the first case in *Radiology* in 1979 and in the *New England Journal of Medicine* (NEJM) in 1980. These publications were followed by a report in 1983 also in NEJM with Dr. Terry. Since HHT is a complex disorder that may involve 1-5 organ systems, it was reasoned that a multidisciplinary team of physicians was required to coordinate their care. The centre therefore follows a multidisciplinary approach, employing a core clinical team of nose, brain, lung, gastrointestinal, and liver specialists to treat the many facets of HHT.

The centre concept for HHT was developed at Yale University in 1988. This center is following 600 patients with PAVM as well as an additional 1000 patients with varying combinations of epistaxis, gastrointestinal bleeding, and liver and brain AVMs. The centre focuses on perfecting new techniques for diagnosis and treatment, as well as understanding the outcomes of therapy. Care is co-ordinated by a genetic counsellor and by Dr White himself, with 100 patients admitted to the interventional radiology service every year and an addi-

tional 100 being admitted to otolaryngology, neurosurgery, gastroenterology, pulmonary medicine, cardiology and general surgery. The decision to employ a dedicated genetic counsellor some 3 years ago has provided the centre with intake histories and pedigrees, coordinated visits, and home care. Dr White gave special credit to the Yale Center's counsellor, Ms. Katharine Henderson, "...whose efforts are extraordinary in their professional input, both as a coordinator of clinics and a research colleague." Patient short stay admissions for the treatment of PAVM, their clinic visits and subsequent referrals have been tabulated below.

#### PAVM patient admissions, HHT clinic visit, referrals 1996-2000

Year	Clinic		
	Admissions	Visits	Referrals
1996	77	167	15
1997	79	170	70
1998	78	158	59
1999	80	177	112
2000	92	180	112

The centre also undertakes student training, with undergraduates working on projects within the organisation and on their own theses. Research into the pathophysiology of AVMs and the genetics of HHT is ongoing and involves collaboration with other centres in other countries.

The Yale centre's clinical excellence and 'educational mission' have made it an organisation that has attracted much international interest, with specialists from places as far away as Thailand, Argentina and Japan coming to Yale to spend a few months learning new techniques. This interest prompted Dr. White to embark upon an impressive international round of visits to hospitals in Denmark, Toronto, Singapore, Malaysia, Japan and Melbourne to name but a few. He spent 10 weeks last summer in Asia doing cases and lecturing. At each location Dr. White, representing the Yale team, because as he says "I am the one with time to leave this long the busy clinical and academic schedule that my younger colleagues follow", lectures, holds clinics and performs embolizations with the staff. He is in fact going to Buenos Aires for one



Robert White in Tongji Hospital in Shanghai

week this September, the same week as the CIRSE meeting, to treat patients and meet other doctors there. The Argentinean hospital's lead physician, Dr. Eduardo Eyheremendy, had spent 3 months at the Yale Center in 1997 but it took several years to get together a critical mass of doctors with enough interest and commitment to form a centre. "We don't visit until there is indication from a group of doctors at prospective centre that they have real interest and commitment to the project," says Dr. White.

This example illustrates the success of the Yale model; as the centre has become more established, other centres began to model themselves after it. As a result of Dr. White's visits, staff members of other hospitals have initiated multidisciplinary clinics of their own for the study and treatment of AVMs. These include, the Universities of Utah, Oregon and Washington at St. Louis in the States and internationally, Holland, Denmark, the UK, Germany, Italy, Canada, Japan and Australia. All of these centers have followed in the footsteps of Yale in developing more specialised care for the treatment of AVMs, associated with HHT as well as sporadic AVMs. The HHT network has had 4 formal scientific meetings to date, the first in Edinburgh (1996), the second in Curacao (1997), the third in

Denmark (1999) and the last this year in April in the Canary Islands, organised by Dr. Claire Showlin, lead respirologist and molecular biologist at the Hammersmith Hospital. About 100 physicians and scientists of all specialities attend these meetings.

A worldwide non-profit organization for HHT was founded in New Haven in 1990. This foundation is called the HHT Foundation International Inc ([www.hht.org](http://www.hht.org)). The



Robert White and Songhua Zhan, lead interventional radiologist at Tongji hospital

scientific board of the foundation consists of fifteen individuals from all disciplines including three interventional radiologists: Dr. Frank Miller who heads the Utah Center, Dr. James Jackson, from the Hammersmith Hospital Center and Dr. White. The non-profit foundation has facilitated the coming together of what Dr. White calls "an extraordinary team of talented clinicians and scientists", working towards the understanding and development of clinical treatment for AVMs and HHT.

Robert White lecturing in Malaysia



## Research benefits from collaboration with cardiologists

*Interventional News* interviewed Jan Peregrin, a lead interventional radiologist at the Institute for Clinical and Experimental Medicine, Videnska in the Czech Republic and organiser of the CIRSE annual meeting in Prague two years ago on the relationship between his department of diagnostic and interventional radiology and the cardiology department.

Peregrin, Pavcnik, Timmermans and Rösch, all leading interventionalists, worked with Jan Sochman on his Percutaneous Transcatheter Aortic Disc Valve Prosthesis. *Interventional News* asked how the collaboration came about. "Jan Sochman and I have been good friends for several years" said Peregrin, "and have done several projects together. He does not have any ambitions to become an interventionalist, but he is extremely skilled in manufacturing small devices and besides that, he is excellent cardiologist." Sochman's comments were in a similar vein. "Me, Jan Peregrin and Joseph Rösch are very good friends and we are probably the 'Last Mohicans' in the field of work on the interventional radiology/cardiology border."

*Interventional News* also asked Dusan Pavcnik what he felt about the collaboration. "We are always doing what is the best for the patients. We cooperate with all specialists including cardiologists. In this case, all are winners, including the patients." Peregrin was also asked why they had approached the CVIR with their work. "The award-winning manuscript is on the borderline between radiology and cardiology and we selected the CVIR for publishing because we considered it of higher quality than other cardiological journals. Jan also believes that radiologists are more open to new devices than cardiologists. I recommended the CVIR because I believed that we are still CARDIOvascular radiologists. And apparently it worked."



Jan Sochman and Jan Peregrin

*Interventional News* asked Peregrin whether he felt the two departments were in competition. "Regarding the turf battles with cardiologists - it is the same problem here as anywhere else. In our institute we have rather specific situation - coronary angiography and PTCA were performed originally by radiologists here and the majority of active interventional cardiologists were trained either by the former chairman of our department, Professor Belan or by me. Now the same cardiologists claim that we are not qualified to perform interventional cardiology. One of my friends used to say "As soon as we showed the cardiologists where the groin and femoral artery were, they do not need us anymore!"



Jan Peregrin and Joe Rösch

As to threats from other specialities, Peregrin felt that so far, interventional radiology was still in a favourable position. "Our position is still strong in this hospital. Apart from a few attempts at carotid stenting, nobody but interventional radiologists are in business." Peregrin's opinions on the future of interventional radiology lie somewhere between Keller's radical proposals and that of the CIRSE President, Dierk Vorwerk. "My personal feeling is that interventional radiology must become a well defined subspecialty even (partly) separated from general radiology and that we must gain our own beds and the possibility to self-refer patients."