

The Centre of Excellence for Hypertension at the HEGP

Summary

Context and history France is the European country in which hypertension is best managed. This result reflects the vitality of the French hypertension school. Paul Milliez was the first to organize the management of difficult cases of hypertension in a department with all the necessary facilities. M Azizi, G Bobrie, G Chatellier, X Jeunemaitre, S Laurent and PF Plouin have maintained the integrated unit at the Hopital Europeen G Pompidou (HEGP) and have extended its activities to clinical research, non-invasive arterial approaches and genetics.

The Centre of Excellence for hypertension at the HEGP The European Society for Hypertension (ESH) has identified centers of excellence (CE) in hypertension. The CE at the HEGP was set up in 2006 and includes the individuals listed above, together with L Amar, M Briet, P Boutouyrie, AP Gimenez-Roqueplo and MC Zennaro. The members of this CE belong to the hypertension unit, the Clinical Investigation Centre, the Clinical Research Unit, the Pharmacology Department, the Genetics Department and the PARCC (INSERM U970). The French CEs are linked together in a network. PF Plouin is the coordinator of the CE of the HEGP and of the French network of CEs.

Why is a CE for hypertension needed? Hypertension requires specialized care when it is severe, complicated, secondary or resistant to treatment. Overall, 80% of the patients referred to our CE have resistant or grade 3 hypertension, and 25% have secondary hypertension (these presentations are not mutually exclusive). Our CE has the capability to perform appropriate biological tests (hormone assays in peripheral blood or in the adrenal veins, genotyping, determination of drug concentrations) for these cases, and has defined reference values and thresholds for intervention. All the facilities for various forms of imaging and telemedicine are also available onsite. In patients with a possible secondary hypertension, our role is to establish the diagnosis and the indication for treatment and to supervise any necessary invasive treatment by interventional radiologists or surgeons. The publications issued from our CE provide patients with precise information about the risks and benefits associated with the invasive procedures undertaken. The role of our CE is also to ensure the training of GPs and future specialists in hypertension. Finally, our mission is to improve knowledge on the pathophysiology of hypertension and its treatments via an active clinical and basic research.

Care policy To limit the waiting time for a first outpatient visit below 15 days, the administrative staff of the CE distinguishes between new patients (from whom clinical information is collected via a questionnaire given before the outpatient visit) and followed patients. Most patients are usually followed by their usual doctor after the intervention or the establishment of a treatment program. In a restricted number of cases, a long-term follow-up is proposed, particularly for patients with severe, complicated or resistant hypertension, polyvascular disease of any origin, renal insufficiency, tumoral disease with a high risk of recurrence or monogenic hypertension.

Networks and reference centers The CE coordinates the following networks for hypertension of renal or adrenal origin and resistant hypertension: ARCADIA/PROFILE (Assessment of Renal and Cervical Artery Dysplasia Register, Progression of Fibromuscular Lesions); COMETE (Cortical and Medullary/Adrenal Endocrine Tumors); DENER-HTN and DERENDIAB (Renal Denervation in Resistant Hypertension or Diabetic Nephropathy); EN2iLA (European Network for Non Invasive Investigation of Large Arteries); PGL-NET (Paraganglioma Network) and the network of French CEs. The members of the CE at the HEGP belong to the National Reference Centre for Rare Vascular Diseases including fibromuscular dysplasia and national clinical expert centers for malignant tumors of the adrenal glands (INCA-COMETE), kidney cancers and von Hippel-Lindau syndrome (PREDIR), and rare endocrine tumors (RENATEN).

Research programs The CE coordinates multiple research programs funded by ANR, INCa, INSERM, FRM, FRHTA, PHRC and which have given rise to hundreds of publications. It is involved in international programs, such as CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions), ENS@T (European Network for the Study of Adrenal Tumors), ENS@T-CANCER (Adrenal Cancer Consortium, FP7 Health 2010), ISPA (Integrated Study of Primary Aldosteronism), INSPIRED (Investigator-Steered Project on Intravascular Renal Denervation) and TNH (Transatlantic Network in Hypertension, the Leducq Network). The CE at the HEGP is the only French center involved in the development of international early (phase I/II) clinical trials for new drugs for treating hypertension.

Publications and teaching activities The CE publishes more than 50 original articles per year. The *h* index for its members varies from 11 to 48. Each year, its members are responsible for teaching for the interuniversity diploma in "Hypertension, a vascular and renal risk" and for giving many conferences at national and international symposia. We have hosted more than 10 foreign doctors coming from various European countries and Canada for periods of at least four months over the last five years.

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1. Context and history

Hypertension is the leading cause of death and disability in Europe and worldwide [Ezzati M et al, Lancet 2002;360:1347], and is likely to remain so for the next 25 years [Kearney PM et al, Lancet 2005;365:217] (see the figures and references in the appendix on page 11). France and the USA are the countries with the best results for management of hypertension in the population, as estimated by the proportion of hypertensive subjects whose hypertension is treated and controlled [ENNS 2006-2007, BEH thématique 2008;49-50: 478]. These results reflect, in part, the vitality of the French school of hypertension specialists in terms of both clinical practice and research.

Paul Milliez, together with Jean-Michel Alexandre, Pierre Corvol, Joel Ménard and Michel Safar, was the first to organize the management of difficult cases of hypertension at Broussais Hospital, where he brought together all the facilities required (hormone determinations, hemodynamics, pharmacology, physiology). Michel Azizi, Guillaume Bobrie, Gilles Chatellier, Xavier Jeunemaitre, Stéphane Laurent and Pierre-François Plouin transferred this unit to the Hopital Europeen G Pompidou (HEGP) and extended its activities to clinical epidemiology, clinical trials and comparisons of strategies, and genetics.

2. The Centre of Excellence for hypertension at the HEGP and networks of excellence

The European Society for Hypertension (ESH) has identified hypertension specialists in Europe, doctors to whom difficult cases of hypertension are referred, and a small number of centers of excellence (CEs) for hypertension, on the basis of medical and scientific quality and technological environment. The CE of the HEGP was created in 2006 and brings together the doctors and researchers listed above, together with Laurence Amar, Pierre Boutouyrie, Marie Briet, Anne-Paule Gimenez-Roqueplo and Maria Cristina Zennaro. Its website can be consulted at www.centre-hypertension.org.

The ESH asked the CE of the HEGP to organize the French CEs into a network and to conduct a pilot experiment in national synergy between CEs. PF Plouin is the coordinator of the CE of the HEGP and the French network of CEs. The organization of the French network is currently seen as a reference for other European CEs.

3. Affiliations

The CE of the HEGP is a transverse structure involved in several larger structures, departments and laboratories of the HEGP. A summary of its affiliations is as follows: AP-HP, HEGP, the hypertension and Vascular Medicine Department, the Clinical Investigation Centre (CIC), the Clinical Research Unit (CRU), the Pharmacology Department and the Genetics Department; the Cardiovascular, Biology and Research Poles; Université Paris-Descartes; and INSERM UMR 970 (teams 3, 7, 13 and 14). The Hypertension and Vascular Medicine Department is the cornerstone of the CE.

4. Why do we need a CE for hypertension?

Clinical background

Blood pressure (BP) is a vascular risk factor and cases of uncomplicated hypertension should be targeted by primary prevention. This notion is, of course, familiar, but the CE, as a tertiary referral center, gives the highest priority to cases of severe, complicated, resistant or secondary

hypertension. Overall, 80% of the patients sent to us by doctors in private practice or at other hospitals have resistant or grade 3 hypertension, and more than 25% have secondary hypertension. These two presentations are not mutually exclusive.

Such patients require specialized treatment, for which we have all the diagnostic and therapeutic resources necessary. These resources are managed in accordance with the French and European recommendations:

- Rapid management of cases of severe, malignant or complicated hypertension
- Ambulatory or home monitoring of BP for confirmation and follow-up of resistant hypertension
- Determinations of peripheral plasma hormone concentrations, both in basal conditions and in dynamic tests, and determinations of hormone concentrations in the renal or adrenal veins. For all these measurements, we have defined reference values and thresholds for intervention.
- Genetic tests for identifying cases of monogenic diseases of the adrenal glands or diseases related to the control of water and sodium balance
- Determination of drug concentrations for the investigation of resistant hypertension
- All the required imaging techniques (CT scan, MRI, angiography, PET scan, scintigraphy, cardiac and vascular echography).

Clinical and translational research

The patient's recruitment, scientific culture and human and technical resources of the CE provide the critical mass necessary for a reference clinical and translational research site. The CE uses the biological resource platform (see the collections of the COMETE and fibromuscular dysplasia networks, page 8) and the technical platform for functional and imaging investigations of the HEGP. Its members are involved in the CIC, CRU and several university and INSERM laboratories. They are also involved in the PARCC (*Paris-Centre de Recherche Cardiovasculaire*; the Paris Cardiovascular Research Centre), for basic research on animal models, cell lines and tissues. The clinical research encompasses epidemiological and genetic studies for diagnostic and prognostic purposes, physiological and physiopathological studies (vascular mechanics, hormones for water, sodium and potassium metabolism) and innovative therapeutic trials (treatment of secondary hypertension, and new drug classes and medical devices).

Training

The CE provides training in all aspects of hypertension for students, residents from various specialties (cardiology, endocrinology, general medicine, internal medicine, and nephrology) and foreign doctors (see page 9).

International reputation

The designation of a CE for hypertension at the HEGP, and, even more so, the coordination of the network of the French CEs, increased the international visibility of the center and the reputation of its members in both academic circles and among industrial partners.

5. The members of the CE of the HEGP

The following doctors, listed in alphabetical order, are involved in the recruitment, investigation and/or follow-up of cohorts of hypertensive patients.

Laurence Amar, endocrinologist, is a hospital and university practitioner from the Hypertension and Vascular Medicine Department. Her clinical and basic research activities focus on endocrine hypertension: primary aldosteronism and pheochromocytoma/paraganglioma (PPGL). She is a member of the national COMETE network, the European ENS@T network and the Special Interest

Group for PPGL of the European Endocrinology Society. She has published 45 original research papers referenced in PubMed.

Michel Azizi, cardiologist, is Professor of Vascular Medicine. He is the scientific director of the APHP/INSERM CIC of the HEGP, and Assistant Head of Department in the Hypertension Unit. He works as a researcher in the UMRS INSERM 970 and is a member of the Steering Committee of the integrated Necker-HEGP CIC for biotherapy. Since 2000, he has coordinated 81 research projects (including 16 international multicenter projects and 26 national multicenter projects) promoted by a public institution in 38 instances (the AP-HP in 21 instances) and the pharmaceutical industry in 43 instances. His research activity focuses on the physiology, physiopathology, genetics and pharmacology of the renin-angiotensin-aldosterone system, a hemoregulatory peptide (AcSDKP) and a peptide involved in water metabolism (apelin). He has developed new strategies for evaluating the effects on BP and hormone levels in humans of new antihypertensive molecules at early stages of drug development (of vasopeptidase inhibitors, renin inhibitors, aldosterone synthase inhibitors and brain aminopeptidase A inhibitors). Finally, he has developed a new translational research and care activity extending from oncology to cardiovascular disease and relating to the cardiovascular and renal complications of molecules targeting the VEGF pathway. Since 2005, he has obtained 18 public research contracts as principal or joint investigator (CIRC APHP, national and regional PHRC, ANR, AO INSERM/DHOS grants). He holds two patents supported by the APHP, one of which, evaluated in humans in 2012, concerns a new, non-isotopic method for measuring glomerular filtration rate. All of his research activities are supported by the CE for hypertension in terms of patient recruitment, and by the associated INSERM units for translational research activities. This research is entirely integrated into the research themes of the CE.

Guillaume Bobrie is a nephrologist and part-time hospital practitioner in the hypertension and Vascular Medicine Department. His clinical research activities focus on alternatives to conventional clinical blood pressure measurement, telemedicine, patient questionnaires and the management of resistant hypertension (PHRC 2005).

Pierre Boutouyrie is a cardiologist specializing in pharmacology. He is responsible for the Clinical Pharmacology unit. This unit comprises a laboratory for non-invasive explorations of the artery wall, a centralized laboratory for the reading and interpretation of hemodynamic results and a data management and statistics team. Its activities are split between the HEGP and PARCC-INSERM U970. The non-invasive investigation techniques are based on the use of applanation tonometry for the measurement of central BP and the speed of the pulse wave, and on echotracking for measurements of the diameter and thickness of superficial arteries and for evaluations of endothelial function. He and his colleagues were the first to demonstrate the predictive value of arterial rigidity for cardiovascular morbidity and mortality in patients with hypertension, to show the modes of arterial remodeling in hypertensive patients and to propose an intermediate phenotype in patients with fibromuscular dysplasia. He has been part of teams carrying out many clinical trials on essential hypertension. His current work addresses the pharmacodynamics of antihypertensive drugs and the factors predictive of a degradation of renal function. He currently works on two large epidemiological projects funded by the *Fondation de Recherche en HTA* (the hypertension Research Foundation).

Marie Briet is a nephrologist and junior lecturer in Pharmacology. She works at the CIC and her research activities focus on the arterial remodeling associated with chronic renal disease, its impact on the cardiovascular prognosis of patients and pharmacological management.

Anne-Paule Gimenez-Roqueplo specializes in endocrinology and molecular genetics. She has been Professor of Genetics since 2008 and practices in the Genetics Department, in which she has established multidisciplinary oncogenetic consultations for endocrine tumors in collaboration with the Psychiatric Liaison Service (K. Lahlou-Laforêt). She is responsible for the molecular oncogenetics

activities of the Genetics Laboratory of the HEGP, an expert laboratory for the molecular diagnosis of hereditary PPGL. She coordinates the national PGL.NET network dedicated to the management of these tumors. Together with H Timmers, she directs the international PRESSOR (Pheochromocytoma Research Support Organization) network and the PPGL working group of the ENS@T network. With PF Plouin, she organized the Third International Symposium on PPGL (ISP2011). She is a member of the national COMETE network and the steering committees of the INCA-COMETE, PREDIR and RENATEN reference centers. Within the PARCC-HEGP (INSERM UMR970) research center, she leads a team working on the genetics of PH/PG. Since 2005, she has obtained 12 research contracts funded by the PHRC, ANR, INSERM, ARC, *La Ligue Contre le Cancer*, APHP or the European Union, as principal or joint investigator. She has published 92 original articles referenced in PubMed.

Xavier Jeunemaitre, cardiologist and geneticist, is Professor of Genetics and Université Paris-Descartes, Head of the Genetics Department at the HEGP and Director of INSERM team 3 “Genes and Arterial Blood Pressure” at the PARCC-U970 HEGP research center. Together with Prof. Jean-Noël Fiessinger, he is also responsible for running the Rare Vascular Diseases Centre of the HEGP, which is affiliated to the Hypertension and Vascular Medicine Department. The Genetics Department holds consultations for genetic counseling and testing for cardiovascular, endocrine and renal diseases and cancers. Its domain of research is mostly the genetics of essential and secondary hypertension. X Jeunemaitre has been principal or joint investigator in many PHRC, STIC and other research projects funded by the INSERM and ANR. He is currently a partner in three European research programs (FP7) and in two transatlantic research programs funded by the Leducq Foundation. He has published more than 250 original articles referenced in PubMed.

Stéphane Laurent, cardiologist and pharmacologist, is Professor of Pharmacology and Head of the Pharmacology Department at HEGP. He directs team 7 of INSERM U970. His research interests include the physiopathology and pharmacology of the arterial system in common diseases, such as hypertension and atherosclerosis and in rare vascular diseases (the Ehlers-Danlos and Marfan syndromes). He has been principal investigator in many institutional and industrial clinical trials. He is one of the cofounders of an international society dedicated to studies of the arterial system (ARTERY). He has founded an international network dedicated to clinical trials in the domains of physiopathology and the arterial pharmacology (European Network for Non Invasive Investigation of Large Arteries –EN2iLA), which currently brings together more than 20 centers in Europe. This network is currently carrying out several clinical trials [PERICLES, CELIMENE, DAPHNET, CASHMERE and Vascular Mechanisms].

Pierre-François Plouin, an internal medicine specialist, is Professor of Vascular Medicine. He was one of the cofounders of the French Society for the Study of Pregnancy-Induced Hypertension. He carried out the first controlled trial of angioplasty for atherosclerotic stenoses of the renal arteries and has participated in two international trials on this subject. He is one of the cofounders and the coordinator of the national COMETE network, a cofounder and member of the Executive Committee of ENS@T, a member of the Steering Committee of PRESSOR, the coordinator of the Endocrine Hypertension Working Group of the ESH and of the PPGL Special Interest Group of the European Endocrinology Society. In the domain of rare vascular diseases, he was the Director of the steering committee for the formalized consensus on fibromuscular dysplasia and is the coordinator of the dozen French centers involved in a research program on this condition (PROFILE/ARCADIA). He has published more than 360 original articles referenced in PubMed.

Maria-Christina Zennaro, endocrinologist, is Research Director at INSERM. She leads the team “Genetic mechanisms of aldosterone related disorders” at the PARCC-U970 HEGP research center. Her research focuses on the genetics and pathophysiology of the regulation of BP in relation to mineralocorticoid hormones, with regard to both their adrenal secretion and their peripheral action. She is also associated investigator at the Genetics Department of the HEGP, where she coordinates

the clinical and research network on type 1 pseudohypoaldosteronism PHA.NET. She is President of the working group on aldosterone-producing adenomas of the ENS@T network, member of the Executive Committee of the International Aldosterone Conference, president of ESAC France, and member of the national COMETE network. Since 2005, she has obtained eight research contracts, as principal or joint investigator, funded by the ANR, FRHTA, ESAC, the *GIS-Institut des maladies rares* (Special Interest Group of the Institute of Rare Diseases) and the PHRC. She has published 70 original articles referenced in PubMed.

6. Reception and monitoring policy of the CE

Organization of the first consultation and telemedicine

Most patients are referred to us by their own primary care physicians or by physicians working at another hospital. When appointments are made, the reception staff distinguishes between new patients consulting for the first time and patients already known to the CE. This makes it possible to ensure that new patients wait no more than 15 days for their first appointment. The CE has established an original procedure for the initial management of patients. New patients receive at home a questionnaire concerning their hypertension, current treatment and medical history for completion, a prescription for the blood tests recommended by guidelines and an appointment with a nurse at which they learn to measure BP at home. The self-recorded BP measures taken by each patient are tele-transmitted, downloaded and printed by the nurses of the CE. All of these data (questionnaire, blood tests, home BP) are thus available to the physician from the CE at the time of the first outpatient visit.

Standardized computerized medical files

The data for the patients are entered into the ARTEMIS computer database. The real-time data entry makes it possible to issue a computerized summary to the patients at the end of each outpatient visit or hospitalization. This computer database is authorized by the French National Commission for Informatics and Liberty (CNIL) and currently contains the medical records of more than 50,000 patients. Specific queries of the database can be performed for scientific purposes or quality audits.

Subsequent monitoring

Most of the patients referred to the CE are followed by their own doctors after a treatment program has been established (for resistant hypertension) or after etiological treatment (for secondary hypertension). Provided the patients and their doctors agree, follow-up is provided by the CE in cases of resistant hypertension or of etiological treatment for secondary hypertension. In a restricted number of cases, long-term follow-up may be proposed: for patients with severe, complicated or resistant hypertension, polyvascular disease of any origin, renal insufficiency, tumoral adrenal disease with a high risk of recurrence or monogenic hypertension.

7. Clinical activity

Complicated hypertension, hypertensive emergencies and other cases

We manage cases of complicated hypertension, which brings us into close contact with the cardiologists, vascular surgeons and neurologists of HEGP. We care for patients with hypertension requiring emergency treatment, including about ≈ 10 cases of malignant hypertension per year. We also take care of patients with unstable hypertension, hypertension associated with orthostatic hypotension, monogenic hypertension (and their relatives), hypertension induced by VEGF pathway inhibitors among patients treated for cancer, and hypertensive children aged more than 15 years.

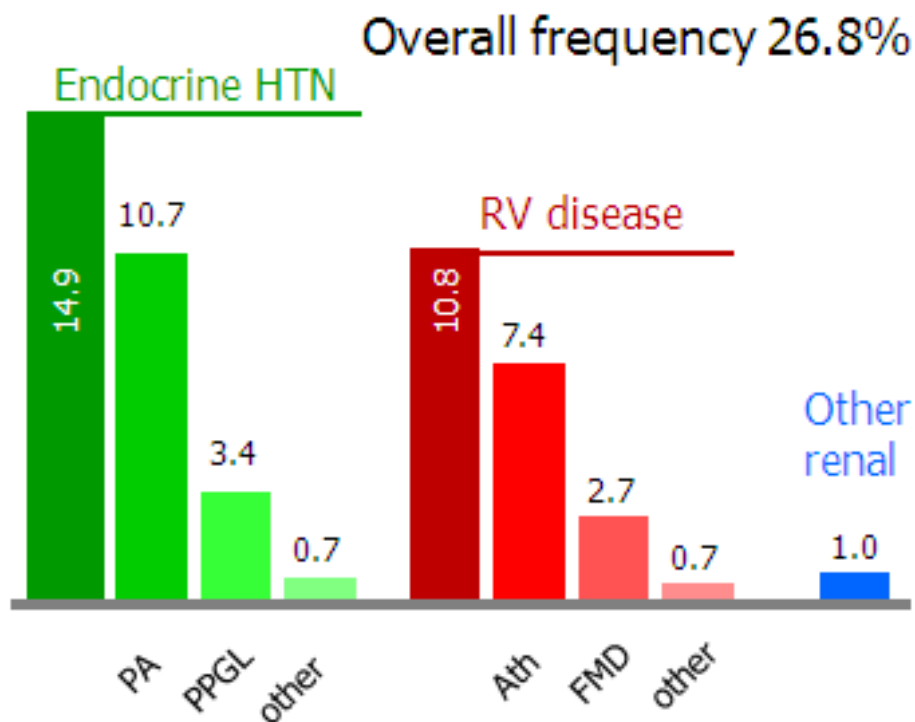
Resistant hypertension

As indicated above, 80% of the patients referred to the CE have treatment resistant hypertension. We have thus established a therapeutic filter period, to better target the population of patients experiencing treatment failure. We have demonstrated the benefits of a treatment with a combination of different diuretics targeting different sodium channels along the renal tubule. We have also participated in an international randomized controlled trial of renal denervation for the treatment of resistant hypertension (HTN-2 trial, published in the Lancet) and have started a national multicenter randomized controlled trial of renal denervation for the treatment of resistant essential hypertension funded by the French Ministry of Health (*Soutien aux Thérapeutiques Innovantes et Couteuses*, STIC).

Secondary hypertension

The figure below shows the proportion of patients with secondary hypertension documented among the 3648 patients admitted to hospital for at least one day from 2005 to 2009. Together with the physiology and radioisotopes department of HEGP, we have defined reference values of various hormones, many of which also serve as national reference values, and intervention thresholds. These investigations also involve various imaging techniques including CT scan, MRI, angiography, PET scan, scintigraphy, cardiac and vascular echography. Long-term follow-up of PPGL organized at our CE has shown a high frequency of recurrence in this disease, particularly for genetically determined forms (more than 30% of cases), necessitating follow-up for an indefinite period.

Percentages of patients with secondary hypertension (HTN) among those recruited by the CE (Ath, atherosclerotic; FMD, fibromuscular dysplasia; PA, primary aldosteronism; PPGL, pheochromocytoma or paraganglioma; RV, renovascular)



Curable forms of hypertension

Many of the patients with secondary hypertension can be cured. This places us in close contact with interventional radiologists (M Sapoval) for renovascular diseases and with visceral surgeons (F Zinzindohoué) for adrenal tumors. Treatment decisions are taken during weekly multidisciplinary meetings of physicians, radiologists, scintigraphists and surgeons with extensive experience of

endocrine, renal or renovascular hypertension. The role of the CE is to confirm the diagnosis and treatment indication, to contact the specialist interventional radiologists or surgeons and to prepare the patients for invasive treatment. Our publications provide patients with detailed information about the risks and the benefits of the procedures performed by our CE.

8. Reference centers and networks coordinated by the CE

Reference centers

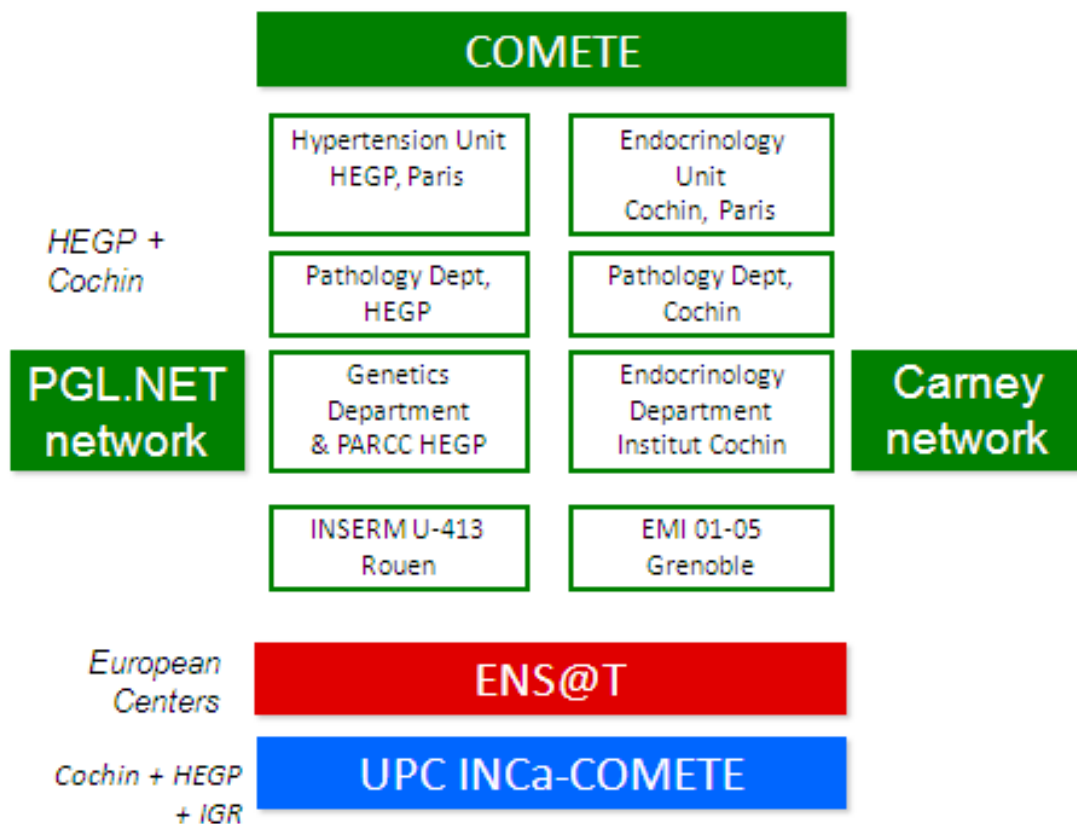
The members of the CE manage or belong to various reference centers:

- The national reference center for rare vascular diseases, including fibromuscular dysplasia, vascular Ehlers-Danlos disease, Takayasu arteritis and Buerger's disease
- The national expert center for the management of malignant adrenal tumors
- The national expert center for the management of kidney cancers and von Hippel-Lindau syndrome
- The national expert center for the management of rare sporadic and hereditary malignant neuroendocrine tumors (coordinated by P Niccoli, Timone Hospital, Marseilles).

Networks for secondary hypertension and rare diseases

The CE runs several networks dedicated to patients with adrenal or renovascular hypertension:

- The COMETE network, which deals with hormone-secreting adrenal tumors (Figure below)
- The PGL-NET network, for patients carrying a constitutional mutation of one of the SDHx genes, resulting in predisposition to the development of PPGL



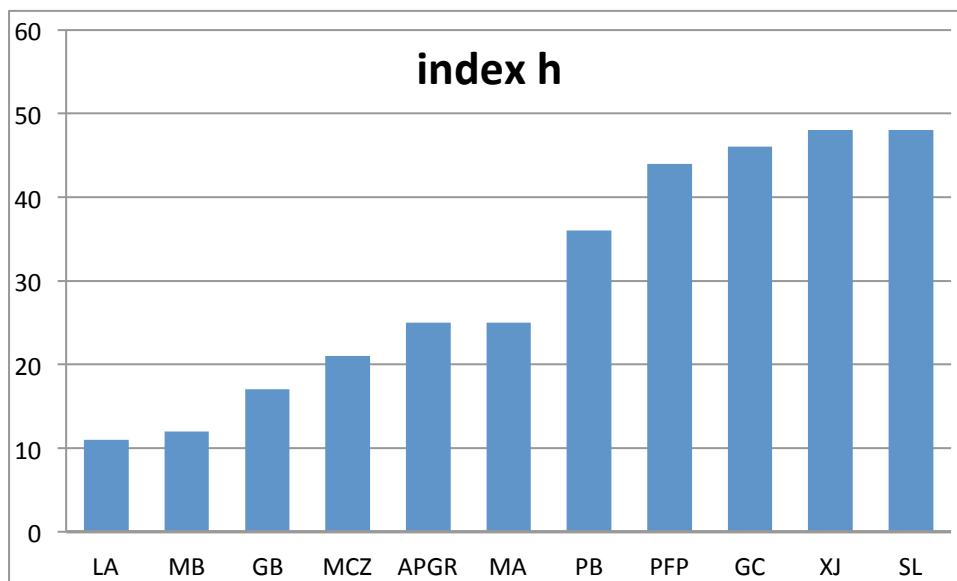
- The ARCADIA/PROFILE network, for patients with fibromuscular dysplasia. This disease affects the renal arteries and supra-aortic trunk. Through the ARCADIA/PROFILE network we are in contact with most of the neurovascular units in France.

The network of French CEs

The CE of HEGP coordinates the network of 13 French CEs created in June 2009 with the support of the ESH and the French Hypertension Society (SFHTA). This network aims to standardize procedures (including those for exploration of the renin-aldosterone system) for exploring secondary hypertension, to promote academic or industrial multicenter trials on hypertension with the support of the national network of cardiovascular CICs, including the CIC of HEGP, to facilitate the mobility of young MDs or PhDs and to share teaching materials relating to hypertension.

9. Publications

The CE published more than 100 articles in international journals in 2011 and 2012. The figure below summarizes bibliometric information for its members.



10. Teaching functions and support for mobility

The members of the CE are responsible for the teaching, each year, of an inter-university diploma in "Hypertension, a cardiovascular and renal risk", which was set up in 2002 by PF Plouin and D Herpin (Poitiers), and for giving conferences at many national and international congresses and symposia. The CE of HEGP runs the network of French CEs, the aims of which include the sharing of teaching materials relating to hypertension and promotion of early-career mobility for young MDs or PhDs.

11. Hosting foreign visitors

The CE has received a number of visitors from abroad in the last five years. Postdoctoral fellows received by the CE over this period were:

- Dr Grégoire Wuerzner from Lausanne, Suisse (November 2006-November 2008)
- Dr Joanna Matrozova from Sofia, Bulgaria (October 2006-January 2007)
- Dr Thierry Gombet from Brazzaville, Congo (November 2006-November 2007)
- Dr Bruno Oliveira from Porto, Portugal (September 2007-January 2008)
- Dr Tiago Gregório from Porto, Portugal (April 2009-July 2009)
- Dr Nathalie Gagnon from Quebec, Canada (January-December 2009)
- Dr Petra van der Linden from Nijmegen, the Netherlands (October 2009-January 2010)

- Dr Hai Yen Tran from Hanoi, Vietnam (January-June 2009)
- Dr Sébastien Savard from Montreal, Canada (October 2010 to June 2012)
- Dr Joana Monteiro from Lisbon, Portugal (April 2012 to June 2012)
- Dr Alessandra Giavarini from Milan, Italy (September 2012 to September 2013)

12. Functions in national and international agencies and societies

The members of the CE are active members of the French Society of Hypertension (SFHTA) and the ESH, and most are members of the International Society of Hypertension. PF Plouin, S Laurent and X Jeunemaitre have been Presidents of the SFHTA, and M Azizi and G Bobrie are elected members of its administrative board. S Laurent has been President of the ESH and X Jeunemaitre has been President of the European Conference on Cardiovascular Research (ECCR). MC Zennaro is President of the working group on aldosterone-secreting adenomas of ENS@T, member of the Executive Committee of the International Aldosterone Conference and President of ESAC France. AP Gimenez-Roqueplo is President of PRESSOR and the PPGL working group of ENS@T.