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Importance of Michel Safar's work for preclinical research

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Michel Safar is a well-known genuine clinician; when you meet him, you rapidly realize that he is completely involved in clinics and in the care of patients. However, he is also a theoretician always searching for a new link between different parameters or a new way to explain an unexpected correlation between apparently independent parameters (if you are or were one of Michel's fellows, you would understand precisely what I mean).

However, if you click "Safar ME & animal" in the Pubmed database, you will find 103 publications i.e. about 25% of his clinical research (on January 2009, this number increases every week...). Michel has never handled a rat or a mouse. I am quite sure that he even never thought to undertake any personal animal experiment; why and how could he have such productivity in experimental research?

First of all, Michel is neither a clinician nor an experimentalist; he is an intellectual who handles concepts; and concepts are the same for understanding both clinics and experimental biology (clinicians speak of "preclinical research"; I would prefer "cognitive research"). Michel believes that schemes, which help to understand both experimental and clinical situations, are good concepts. Second, Michel always tries to convince his young clinician fellows to join an experimental team and to ask clinical questions to experimentalists. It is striking that all Safar's fellows have or have had an experimental activity.

What did Michel Safar provide in the experimental field? We can split his work into two periods:

- 1979 to 1998: His first preclinical publication in the first volume of *Hypertension* and with a premonitory title: "Essential hypertension: an approach to clinical data

by the use of models".¹ During these first 20 years, Michel mainly studied the sympathetic tone, the renin-angiotensin-aldosterone system, and the large artery structure–function relationship in hypertensive models. He revisited the concept of arterial stiffness as early as 1980 and raised the question of the importance of the arterial pulse pressure.

- 1998 to today, Michel Safar extended his works in hypertensive animals to the role of the endothelium in the control of blood pressure, arterial and cardiac fibrosis by drugs and hormones, and he widely developed the use and understanding of measurements of arterial stiffness (compliance), pulse wave velocity and pulse pressure. In 1988, Michel was involved in the first publications introducing the new concept of arterial remodelling in relation with hypertension and treatments in the rat and in patients.

Arthur Guyton's theories are very familiar to Michel Safar and during the last 40 years, Michel was always, and may be overall, interested in the role of Na and in the kidney function in hypertension. I guess that with the understanding of arterial hemodynamics with D. McDonald and M. O'Rourke, these two questions were the mainstream of Michel Safar's basic research.

Reference

1. Chau NP, Safar ME, London GM, Weiss YA. Essential hypertension: an approach to clinical data by the use of models. *Hypertension* 1979;1:86–97.