Rev Clin Esp. 2014;214(7):418–421

Revista Clínica Española

www.elsevier.es/rce

HUMANITIES IN MEDICINE

On being a Doctor . . . and work in Harvard

Ser MÉDICO . . . y trabajar en Harvard

Biography

It is fascinating to reflect retrospectively on which courses, which lectures, or which clinical rotations defined our professional careers the most. For me, they were probably Biostatistics by Prof. Jose Luis Carrasco, Clinical Trials by Dr. Fernando Garcia Alonso, and my weeks at the Clinical Genetics Department. Not to forget all other faculty and departments at the Facultad de Medicina at the Universidad Autónoma de Madrid and La Paz Hospital, where I grew up and that I remember with such gratitude and affection.

I graduated from Medical School in 1995, when the Médico Interno Residente (MIR) exam was going through turbulent changes. That facilitated my decision to pursue formal training in research methodology. With funding from the Real Colegio Complutense I obtained a Master's degree at the Harvard School of Public Health (HSPH) in Boston, United States. Those 9 months at Harvard showed me how much more was there to learn. The Department of Epidemiology accepted me into the Doctoral Program and financed my training. And so it goes, I continued down an academic path. In my thesis I integrated my interests in both drug safety and embryology to study the teratogenicity of folic acid antagonists. In 2000, I accepted an Assistant Professor position to continue my studies on drug safety during pregnancy at the Slone Epidemiology Center at Boston University, under the mentorship of Dr. Allen Mitchell, a pioneer in the field. In 2005, Harvard offered me a faculty position at the Department of Epidemiology, where I currently combine research and teaching activities.

Work at the Harvard School of Public Health (HSPH)

The mission of HSPH is to ''advance the public's health through learning, discovery, and communication''. To pursue this mission, the School produces knowledge through research, reproduces knowledge through higher education, and translates knowledge into evidence that can be communicated to the public, policy makers, and practitioners to advance the health of populations.'' Faculty at HSPH is expected to contribute to these three pillars; and to raise their own funding to support research projects. Students at HSPH are trained to be T-shaped leaders, i.e. leaders with knowledge that extends to many areas of public health and is deep in a few areas. My area of concentration is Pharmacoepidemiology.

Pharmacoepidemiology Program

I have been the Director of the Pharmacoepidemiology Program at HSPH since 2005. The Program was established in 1986 by Professor Alexander Walker. The goals of the Program are to advance research in the safety, effectiveness and utilization of drugs, vaccines and medical devices; identify and develop data sources and methodology for pharmacoepidemiology research; and prepare talented students for leadership in the field. The achievements of our graduates, who currently occupy key positions in the government, corporations, and academia, speak for the value of the Program. We have been able to support doctoral students

http://dx.doi.org/10.1016/j.rce.2014.03.012

Figure 1 Harvard Graduation Ceremony 2013. I am with the famous cellist YoYoMa.

and postdoctoral fellows thanks to the generous support by the Pharmaceutical Research and Manufacturers of America training grant, the Millennium Fellowship, the Asisa Fellowship; and contributions from Pfizer, Bayer, and Analysis.

Life at Harvard

Harvard is more than a work place, it is a vibrant multicultural intellectual community. The interaction with peer students, fellows and faculty leads to long-standing networks around the Globe. There are ''once in a life time'' opportunities daily, from social events where you meet colleagues with a wide range of interesting backgrounds to inspiring lectures by World leaders. For example, I recently attended an event where President Bill Clinton was honored by HSPH, and a lecture-performance on the musical history of the roots of jazz in New Orleans by Wynton Marsalis at Sanders Theater.

The problem is finding the time to enjoy so many opportunities (Fig. 1). The flexibility of academic careers can be both a blessing and a curse. On one hand, to some extent, you can work at your own schedule. On the other hand, there is also certain expectation to work 24/7 and without vacations. As an example, it is common for faculty to send requests on Saturday evening; and for co-investigators or advisees to respond before dawn on Sunday. Not that you have to, but most people do it. However, we rarely complain about too much work, just about the days being too short to do all the things we would like to do. Uncertainty is certainly the worst aspect of academic life nowadays. At HSPH, you have to raise around 80% of your salary with research grants, as well as the salaries for your team and other study

Figure 2 Harvard life may start early in the morning, removing snow from the car.

costs. Given the cuts in federal funds for research in the last decade, securing your salary has become a nightmare.

However, what defines my daily life is not being at Harvard, or living in Boston, but being a woman ''balancing'' professional and family lives. (Ah, yes, personal life too, I forgot.) Let me give you an example of a couple of days in our life. We live in Brookline, a little town adjacent to Boston with good public schools and small coffee shops, bakeries, ethnic restaurants and bookstores. I wake up at 7:00, prepare breakfast and pack lunch for the kids, get them out of the door by 7:45 and drop them at school on my way to work, before 8:00 (Fig. 2). During my 30 min fast walk to HSPH I listen to music and plan the day. After greeting the security guard at Kresge Building, I grab a coffee, and go to my 8th floor office, from where I can see the Harvard affiliated Hospitals. I first screen my email. I am still learning how to control my inbox. One strategy is blocking hours to think and write grants, manuscripts, reviews or presentations. After 10:30 I typically start having meetings with students, post-docs, and research teams in my office; or larger faculty meetings at the Department or School level. From 12:30 to 1:30 I eat my lunch in front of the computer or while attending a seminar. In the afternoon I may have teleconferences with national or international collaborators from academia, government or industry. During the semesters when I teach courses, I then concentrate on reviewing the lecture that I will teach from 3:30 to 5:25 to around 100 students taking the course on study designs. Time to run back home, where

a babysitter or the after school program have been taking care of the kids since they finished school at 2:30. In my lucky days I stop by the gym on my way to work and take a Zumba class. (I love dancing, it is my favorite exercise and anxiolytic.) Kids have activities almost every day, and the logistics when you have two boys can be challenging. Parents here do ''car-pooling'', i.e. take turns to drive 3 or 4 kids. At home, we supervise the kids' homework, cello and piano practices. I cook dinner Spanish style, with olive oil, and we eat together. We do not have TV. The kids go to read and sleep around 9. After organizing the house, there are two more hours to work on the computer before the brain runs out of batteries.

During weekends there are usually one or two kids' soccer games, an outdoor activity around Boston (hiking, biking, skiing, canoeing), and a relaxing movie evening at home. We also enjoy having friends home for dinner and, from time to time, memorable large parties that can end up with Professors and Students dancing and singing together with videogames. During school vacation we visit family in Madrid. In addition, one of our favorite hobbies is traveling and discovering new activities, like scuba diving.

My research

I investigate the safety of medications, with a focus on drug safety during pregnancy.

Based on its molecular structure or class, one can often predict a drug's adverse effects, which typically result from its pharmacologic or toxicologic properties. This is not the case for teratogenic effects, since we rarely know the mechanism by which a teratogen causes birth defects. Indeed, despite intensive laboratory research, we still do not know the biological mechanisms for the effects of even such well known teratogens as thalidomide and isotretinoin. Without the ability to rely on a drug's structure/function to predict its teratogenicity, one would hope to identify these effects in animal studies. However, animal studies are seriously limited in their ability to predict human teratogenesis, both because of considerable variations in teratogenic effects even among mammalian species and because results at the dose levels used in animal toxicology studies may not predict those that might be observed at the intended therapeutic doses. Exposure to humans in pre-approval studies offers the last opportunity to identify teratogens before drugs become widely used. In theory, such studies, although small, might be able to detect the most devastating teratogens, but in practice, for ethical and legal reasons, pre-approval trials usually exclude women who might become pregnant, particularly if there is any suspicion from animal studies that a drug might be teratogenic. Therefore most maternal and fetal toxicities are identified *only after* a drug has been marketed and used by pregnant women who become, for all practical purposes, therapeutic orphans.

Post-approval epidemiological studies provide the primary mechanism for identifying potential teratogenic effects in humans. I conduct this type of studies to produce the evidence necessary to improve health outcomes in pregnant women and their offspring, and to develop drug regulation and clinical guidelines. My ultimate goal is enabling women who are either pregnant or planning to be pregnant to make optimal decisions and move forward in their lives with the least risk and the most benefit from the medications they need.

I evaluate preferentially the safety of drugs with the highest clinical and public health impact. These drugs can be classified in three groups: (1) medications with suspected teratogenic activity (e.g., folic acid antagonist), (2) medications that must be taken by pregnant women to control conditions potentially harmful for the fetus (e.g., antiepileptics), and (3) most commonly used medications (e.g., antidepressants). Some specific questions that we investigated included whether periconceptional exposure to drugs that are folic acid *antagonists*, which include such common drugs as trimethoprim, might *increase* the risk of neural tube defects and other malformations.[1,2] For anticonvulsants, we intend to determine the safest therapeutic regime for women of childbearing age.[3–6] We have also assessed the comparative safety and effectiveness of specific antidepressants by pregnant women.[7–14]

The Future

The new focus of multiple health care institutions on patient-centered issues encourages research that would help fill gaps of information in clinical practice. Evidence based information to manage medical conditions in pregnant women, and women of childbearing age, is missing. My intention is to keep generating actionable evidence on the safety of drugs for pregnant women, as well as applying advanced epidemiological methods and developing new methods when needed. New groups of medications I plan to study include antipsychotics, opioids and other pain medications, and antidiabetic medications. My goal is to apply comparative effectiveness (and safety) research methodology to questions that are directly relevant to pregnant women and their health care providers.

My life in 2024

I spent my first 10 years in Boston saying that I was going back home in 2 more years. I stopped saying it, although I still feel that I will go back to Spain one day. Professionally, I hope to continue enjoying my research. From Harvard, or from other institution, I will continue my collaborations with the amazing colleagues I met on my way. However, administrative responsibilities will likely represent a growing proportion of my time, since employees tend to ''rise to their level of incompetence''. Personally, my kids will be ready to fly on their own. Assuming good health, I plan to replace their activities with mine and resume going to the ballet, opera, theater, restaurants... and diving into the deep blue see.

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