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Entrevistas

**Marshall David Lindheimer**

**Dr. Marshall David** Lindheimer was one of the speakers at the 7th Paulista Meeting of Nephrology, held in Campinas-SP, Brazil, last September. On his way to Campinas, he spent two days in Brasilia, Brazil\'s capital, invited by the Nephrology and Obstetrics/Gynecology local Societies. During his time in Brasilia he was interviewed for MedOnLine, a Brazilian Electronic Medical Journal, by three nephrologists (Marcelo M. Almeida, Adolfo H. Simon and Istenio F. Pascoal) and one obstetrician (Claudio B. Pedrosa). Speaking frankly and intensively about science, medicine, family, education, politics, culture, future, life and death, it turns out to be a superb interview. Enjoy it!

***The Editor***

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**IFP** – Dr. Lindheimer, thank you for this opportunity to interview you. We begin with the traditional question we ask to all interviewees, that is could you give us some insight into your origins?
**MDL** – I was born in Brooklyn, New York, in 1932, when the United States had just entered the great depression. However, my parents were schoolteachers in New York City and ironically schoolteachers during the depression were near the top of the pay scale in the United States. Thus we lived comfortably, and did a lot of travelling because teachers have a two month vacation each year. Thus I saw a lot of America, and despite my youth still retain memories of the great depression in the United States.
**AHS** – Why did you decide to study medicine?

**MDL** – I received my undergraduate (BA) degree from Cornell University, and following graduation I was drafted into the Army during the Korean War, but did not leave the United States. Upon completion of my military service I became eligible for what was called the "GI Bill", that is a government subsidy for further education. At that time I had few thoughts of a career in medicine as my undergraduate degree majors were in Philosophy and Zoology at Cornell. My initial thoughts were to seek a career in government, perhaps at the State Department. Thus I

spent a year in Philadelphia at Dropsie College for Hebrew and Cognate Learning, a school where one studies subjects such as Egyptology, and in my case Middle Eastern affairs. But, several events led me to change my career goals. The major one though was that this was the 1950s, and well before the “Kissinger” era at the State Department, and few Jews had a chance for successful careers there as Middle East experts, given the State Department’s closeness to the oil lobby and their concerns regarding the oil rich Arab nations, especially during the “cold war”!!

**CBP** – Did your parents influence this decision ?

**MDL** – No, absolutely not. At that point, somebody remarked, don’t you know that you can use the GI Bill stipends to study in Europe? I said: where can one go to? He said: it is easy to obtain admission to the medical school in Geneva, Switzerland, and the dollar was then fixed at 4.25 Swiss francs. I went. When I started to study medicine I was still a bit of playboy (smiles), but I discovered an area that I liked very very much, became a serious student, and actually led my class in Geneva. There, I also met my talented and wonderful wife Jacqueline. Of interest, in those days one had the option of transferring back to a US medical school, after one’s first two years, dependent on passing part one of the National Boards, and several American students in my class did so. However, my father-in-law felt that he would never see his daughter once she went to live in the US, and I stayed in Geneva for the whole five years (and actually taught a board cram course for my American colleagues applying for transfer). The reason I am telling you this history is that after returning to US, at every stage of my initial career, and until I joined the faculty at the University of Chicago, I had to do everything twice as well as US trained colleagues, and every mistake I made was attributed to my foreign medical training. Thus, I have considerable empathy for the foreign medical graduates, and am ashamed of the way the American medical establishments sometimes treat them.  Now, let me answer your question more directly. My parents were schoolteachers, and being the first generation of immigrants to the US...

**MMA** – Immigrants from where ?

**MDL** – ... Well, my four grandparents came from Poland, Russia, Germany and France. This is the typical American melting pot, and you have a similar big melting pot in Brazil. The first generation worked very hard, their children became schoolteachers and all these schoolteachers wanted their children to be a doctor or a lawyer, but I really became a doctor without direct pressure from my parents.

**IFP** - What about your training once back in US?

**MDL** - I did my Internship in Rochester, NY, and my residency in Internal Medicine in Brooklyn, NY, finishing as chief-resident at Brooklale Hospital, where Isador Snapper, a luminary in Internal Medicine at that time, was chairman. It was through Dr. Snapper that I was accepted as a trainee at Boston University, sponsored by Norman Levinsky, who was then at the Metabolism and Electrolyte section (if I remember correctly), headed by Arnold Relman. These were the early days of nephrology (we had neither hemodialysis nor transplantation), and I was funded through a United States Public Health Service fellowship (now it would be called an NIH fellowship). After two years, I went to the mid-west,.initially in Cleveland (Case-Western U) for three years, then at Northwestern University in Chicago for one year, and finally, in 1970 I was recruited to the University of Chicago, where I remain until this day. At the moment I am talking to you I am in the midst of a six-month award as “The Francqui Foundation International Visiting Professor”, in Leuven, Belgium. My appointments are not only in Medicine, as you know, but also in Obstetrics and Gynecology and in Clinical Pharmacology.

**Foto: Dr. Lindheimer**

**MMA** – Why did you choose nephrology?

**MDL** – Early in my career I wanted to go into academic medicine, including research. In the late nineteen sixties the leadership of most Departments of Internal Medicine were all nephrologists, such as Seldin, Welt, Papper, etc, a little later Early, Relman etc, and medical students and residents were attracted to the nephrologists to learn the mysteries of electrolyte disorders and of acid base. Unfortunately, now they all are running to the intensivists, who teach them formulas rather than thinking. Thus, this is probably why I sought a nephrology fellowship in Boston.

**CBP** – If you were at the beginning of your career now, would you make the same decision? When did you become interested in obstetrics?

**MDL** - Well, I don't know... because I am not at the beginning of my career (smiles). But my interest in obstetrics is a funny story too. When I started out in nephrology, the big issue was looking for natriuretic factors. For instance, DeWardener, Levinsky, Early, and others were feverishly and competitively working in that area. In those days, the natriuretic factor we were looking for, the one that controls the kidneys to excrete salt, was called "third factor". It was called "third factor" because an experimental situation was set up like the one in Levinsky's dog laboratory, where an animal with an aortic clamp received aldosterone and/or other corticoids to eliminate the humoral factor. The clamp around aorta was used to decrease the glomerular filtration rate (factor two). The dog received a salt-load and then the GFR was decreased by the clamp, and continued to receive mineralcorticoids all through the experiment. So, if the dog's urinary sodium excretion was still increased over the preexpansion baseline levels, it was not due the first factor (hemodynamic) or the second factor (mineralocorticoids). It had to be another natriuretic factor that was called "third factor". One day, when reading some medical literature, I came across renal studies in pregnant women that demonstrated that when in late gestation a gravida turns from her side to her back, the enlarged uterus drops on the vena cava, and this decreases glomerular filtration rate. Of course, in those days as in now, one could not design experiments on humans using an aortic clamp to decrease GFR (smiles), I said: Ah, pregnancy is my human aortic clamp! Afterwards, I sought collaborators in obstetrics to see if I could arrange studies where, following a saline load one could decrease the GFR of a pregnant woman by changing her posture, just as a model to study the third factor. When one is a physician-scientist seeking to do some human physiology studies, you just do not do pure research, but one walks around the wards, and looks at some of the problems related to your discipline. So, though I had become interested in designing just a single experiment, I found an area in which research relating to disease was sorely needed and an area of reproductive medicine that interested me very much. My career since then has focused on renal function, control of blood pressure and volume homeostasis in both normal and abnormal pregnancy. Also, if you're going to work with pregnant women it is best to also be in a Department of Obstetric and Gynecology. Thus, I spoke to Fred Zuspan, who recruited me to the University of Chicago, where I have done the bulk of my clinical and basic science research related to the kidney in pregnancy, and have been involved in the care of pregnant women with a variety of medical problems as well for the past 30 years.

**MMA** – What happened with that old glamour in nephrology ?

**MDL** – Well, I still think that nephrology has a lot of glamour. I am aware that the academic nephrology world is worried because house-staff seem to have lost interest and less of them are seeking fellowships and/or academic careers in nephrology. Some of that may be due to a misconception by some that there is a cap on the amount of nephrologists needed in the US, that there are too many subspecialists in general , and that the way to go these days is as a generalist. There are exceptions such as gastroenterologiy and cardiologiy that are better paid, or compared to dialysis physicians may provide one with more free time! primarily because subspecialists in these two areas perform lucrative procedures, but I don't think these views are permanent. There are always cycles in medicine, and I suspect that at some point interest in nephrology will return (or the discipline will face a severe shortage, which may also make it more lucrative and increase interest!!).

**AHS** – But at the present time we might be on the depressive phase of this hypothetical cycle in nephrology. In your opinion, should this be attributed to the nephrology itself or to the way that nephrologists are doing nephrology?

**MDL**– Let me focus on academic nephrology first. For sure, the increasing absence of bed side luminaries, not only in nephrology, but in all academic medicine, is one reasons for a crisis. We are losing our physician-scientist-role models in clinical academic departments. Some people note that in the past, for example, it was possible to have double or triple threat stars. People who could compete successfully in a basic science lab and were also sterling teachers and clinicians at the bedside... In my time Donald Seldin was a great example of such a star. Such luminaries, "showmen", or role models, energized students and house-staff, and inspired some of them to seek academic careers. Now, to succeed in academic medicine, you can't do "three or even two at once" and many of the people who could be potential academic role models, leaders and teachers tend not to go to the clinical departments anymore, where they can teach and observe disease at the bedside, but seek careers in basic science departments instead We have to create the conditions that make such people return to our departments of Medicine, Surgery, Obstetrics, etc, and not go full time to Cell and Molecular Biology departments. I am among those who believe that there is still a lot of charm related to all aspects of nephrology. If we can stimulate one out ten students, that is all we need.

**Foto: Drs: Marcelo, Istênio (left), Dr. Lindheimer (center) and Drs**

**Cláudio e Adolfo (right)**

**IFP** – What is the present balance and tendency between basic research and clinical work? Are they parallel or divergent?

**MDL** – It changes from country to country. In the US we have a lot of private medical schools, where the Clinical Departments have been

forcing faculties to do more and more clinical works, particularly to earn professional fees from private patients. This is making them less competitive for obtaining grants, and provides them with less time to try to emulate the Seldin-like role models of the past. It is also contributing to disturbing statistics such as that there are less and less students now graduating from the medical school who want to go into research, and those who do believe it is much easier to be in a department where they do not need to do clinical work in order to successfully complete grants. Also in the era of molecular biology such people tend to go more and more into basic science departments. But I think what we have to do is bring them back to clinical departments, and give these people the time and opportunity to succeed in their research careers.

**CBP** – Are pharmaceutical industries playing a positive role by sharing research projects and policies with the universities?

**MDL** – People within our clinical academic communities are looking for solutions such as that. I am one who is not very happy about the fact that more and more research from industry have been set up in academic centers, because when you work with industry the openness of sharing thoughts of research may be compromised. I don’t really know what the answer is, but I guess the answer still is that academic hospitals at the universities have to realize that a certain amount of their resources should be to stimulate research in the clinical departments, including nephrology, realizing that this will certainly result in a better future, or to convince the “CEOS” who now run many of these clinical centers, in contradistinction to academic visionaries who should, that when they support disease related basic research in clinical departments they are investing in reducing the costs of medical care some times in the future.

**IFP** – At the University of Chicago you are Professor of the Departments of Medicine and Obstetrics and Gynecology (and also member of the Committee of Clinical Pharmacology). On the daily basis, which side do you feel closer to?

**MDL** – I would like to say that I am constantly working in both departments. To me it has been very important to actively participate in the Department of Obstetric and Gynecology - even though much of my patient care service, like clinics and rounding, takes place in the Nephrology section. As an example, when consulting on medical problems in pregnancy it is critical to understand how obstetricians work. Here, unlike many of my colleagues, no matter how strongly I feel about a case I am consulting on, I will tell the obstetrician what the options are, but never demand he or she accept my recommendations. Of importance, I never tell an obstetrician that he or she has to deliver a baby. This is but one example of what I have learned through the years of being in the obstetric department at my university. For instance, it is very easy to examine a patient for one hour and say what is going to happen, and what should be done, while the obstetrician has followed the course of the patient for nine months and often is under pressure to make rapid decisions, and is the one responsible for the outcome of two patients. These decisions, may have to make quickly and should take place without adversarial pressure. I may have strayed from the question, but it is an example of what a nephrologist learns from being in another department.

**AHS** – At the end of this millenium, why is the etiology of preeclampsia yet to be defined?

**MDL** – First of all, you should understand that less than 25 years ago, research in preeclampsia was still sporadic, people from different disciplines rarely met and very little research funding went to study the problem. The International Society for the Study of Hypertension in Pregnancy was only founded near the end of nineteen seventies. All of this “lethargy” was present despite the fact that preeclampsia was and remains a leading cause of morbidity and mortality to both mother and fetus. Like many problems in medicine, once some of us started to focus on the problem, and alerted scientists and a few funding agencies

to the needs relating to understanding, preventing and managing this malicious disease, an exponential increase in the amount of people doing research, and in the amount of progress made in the field followed. Thus we are now a lot closer towards unraveling the pathogenesis and pathophysiology of preeclampsia. Every year the quantity of publications in the area increases enormously, including the content of the Biannual Meeting of the organization I just mentioned. I would not be surprised if some of these questions would be answered at the start of the next millenium. Those interested should know that next meeting of the International Society for the Study of Hypertension in Pregnancy will be in Paris, July 2000. These are usually exciting meetings that too few of my fellow nephrologists attend. Perhaps you may find an answer to your question there (smiles).

**CBP** – Based on what we know from the pathophysiology of the preeclampsia, would you consider the fetus him or herself integrated into the etiology and/or pathogenesis of preeclampsia?

**MDL** – There are pathophysiological features of the disorder that involve the fetus, and one, intrauterine growth retardation may be one link towards our understanding the cause of preeclampsia. So, your hypothesis is very sound.

**AHS** – Taking this hypothesis as valid, how could be explained the fact that molar gestation where there is no fetus has a high incidence of preeclampsia?

**MDL** – First, there are people who believe that the etiology of preeclampsia is heterogeneous, while, others think that the placenta is the area where the origin of preeclampsia lies. Molar pregnancy is a good example of the second postulate for as you noted it is associated with substantial preeclampsia. Here the relatively avascular large placenta associated with hydatiform mole easily fits the theories of those who state that placental ischemia leads to the pathogenesis of the disease.

**IFP** – In the last 30 years there has been at least four attempts to prevent preeclampsia, such as: salt-restriction, diuretic therapy and, in the last ten years, aspirin and calcium supplementation. All of these efforts seem to have failed. What happened and what would be the next step to prevent preeclampsia ?

**MDL** – I think all these failures are examples of rushing too fast when there was a paucity of basic research data on the etiology of preeclampsia. Often, based upon some small amount of data, and a hypothesis still to be proven, people have proceeded directly to large and expensive prevention trials, aspirin and calcium being examples of this. I always felt that most of our resources should go in to establishing the cause of preeclampsia definitively before we do all of these studies on the prevention side. Actually if you look at the last week issue of Lancet, there is a small study suggesting that Vitamin E and Vitamin C can prevent preeclampsia in high risk patients, the hypothesis being the abnormal relationship among circulating oxidants and anti-oxidants in preeclampsia. I would not be surprised that some will now jump into a large multicenter trial to test this hypothesis, but, again, before spending that money we should be looking for more definitive data. But, in reality, I am sure that the next step in the history in preeclampsia prevention trials will be studies of Vitamins E and C, and you may wish to check the prices of the vitamin producing industry's equity on the stock market (smiles).

**Foto: Drs Istênio, Lindheimer and Cláudio**

**CBP** - Are you satisfied with the theory of failure of trophoblastic invasion of the uterine spiral arteries as an explanation to etiology of preeclampsia?
**MDL** – This is not my area of research, but people like Professor Pijnenborg, in Leuven, for example, have done a lot of work in this field. One of the leading reasons for the hypothesis that placenta is the cause of preeclampsia is observation of a lack of trophoblastic invasion into the myometrial part of the spiral arteries leading to relative ischemia, which might be responsible for preeclampsia. It is a highly attractive hypothesis, and a great deal of research is now being performed based on these observations, such as seeking links with this phenomenon and the production of certain cytokines that enter the maternal circulation and damage the endothelium, as well as the role of circulating proteins produced by the placenta such as inhibin and activin, as markers to predict patients at risk. It is a very fascinating area and we will see more research on it in the next decade.
**AHS** – Let's move to a new scenario. Have you ever tried any sort of alternative medicine to treat yourself or some of your relatives ?

**MDL** – No, I have never tried any of these methods, but I am aware of the fact that alternative medicine has become very popular in this recent decade. This is, in part, due to the fact that people are increasingly mistrusting physicians and are ready to listen to loquacious individuals on the benefits of alternative medicine. I think that everybody should keep an open mind, because we are in the age not of alternative medicine, but of evidence-based medicine. If you look carefully at and make critical analysis, most of alternative medicine studies turn out to be a very poor literature. So, if there is a future for alternative medicine, people there have to do better research first to convince us.

**IFP** - How would you like to die ?

**MDL** - This question is a bit morbid....

**IFP** - I understand, but...

**MDL** - ...but If you insist, my answer is: Like everyone, peacefully, painlessly, and rapidly.

**MMA** – If you were not a physician, what would you like to be?

**MDL** – There are two answers for that. All of us in academic medicine face hard competition for grants, and when things are bad, I get a little depressive, and want to be a cabinet maker (smiles). But, in reality, the other area that has always interested me - sounds horrible for a physician to say that - has been law. Whenever there is a television, show, for instance The Practice, or a movie that stresses court room drama, like Ten Angry Men, I run to watch them. Of course, the University of Chicago has a very eminent law faculty. However, being at the end of my career, your question is one that is very hard to answer, particularly what my thoughts back in nineteenth fifties would have

been. As I told you at the beginning, I started out wanting to go to State Department to handle Middle-East affairs!!

**Dr. Lindheimer**

**IFP** – As I know you have always been a very hard worker, walk-in at the Hospital at 6:00 AM, leaving at 6:00 PM. Do you have any hobby or favorite entertainment beyond of practicing medicine?

**MDL** – My interests outside of medicine have been mainly reading, but I also like to travel, especially travel that may have a cultural aspect, and my wife has encouraged me on that. But, one thing that I have tried to do, no matter how much the workaholic schedule is or how many obstetric journals I have on the left side and nephrology journals on the right side, is to read 6 books a year, including novels (currently Angela's Ashes), biography (Churchill, De Gaulle, etc). I think all academic physicians who are workaholic should try this.

**MMA** – What about movies?

**MDL** – I cycle. There are periods movies interest me and I go to theaters frequently, and there are periods I see few, and currently I think the quality of movies is poor. I have always been a big fan of Woody Allen, but I never look at people's personal life (smiles). As I mentioned, I like court room themes, also mysteries and comedies. When I want to relax I do not like tragedies.

**CBP** – Let's talk about marriage? What are your feelings about marriage nowadays?

**MDL** – I believe in marriage, at least since 1958 (smiles). Most of people who know me in academic world call my wife Jacqueline "the saint" (smiles). It is interesting that opposite personalities usually do well. My wife has never had an interest in medicine, she is the artistic part of family being a cellist. We have five children, most of them have gone more or less her way and none of them went into medicine.

**AHS** – Does it mean that she is the strong model of the house, even when you are the well-respected scientist?

**MDL** – Sometimes when we used to talk about physicians and academic medicine, my children said they never saw their father (smiles).

**MMA** – Do you have grandchildren?

**MDL** – Yes, two. I have one grandson and one granddaughter.

**MMA** – How old are they?

**MDL** – The granddaughter is 3-months old and the grandson... I believe... has just turned seven.

**AHS** - What would you like them to be?

**MDL** – Happy.

**IFP** – Beyond being happy, what should they be doing in the future?

**MDL** – What they like. I never really had much say strategically when rearing my children. The reason is because my wife was always afraid that I would be a Jewish mother. That is she was afraid that if they received a grade of “A minus or 5.5”, I would asked, what happened to the minus or to the other half of a point? Thus their report cards were kept from me. Only on one occasion, she showed me the report card of one of my sons as it contained an A. I said how wonderful, the grade was for physical education (smiles). My children were never given an allowance either. Sometime after toilet training, Jacqueline gave them a monthly sum with which they had to buy cloths, and meet most other needs, and if they ran out of money in the middle of the month tough! They have grown up to be quite independent and resourceful.

**CBP** – If you could change something in American political life, what stone would you move?

**MDL** – I am still one of physicians who believes that healthcare is a right, not a privilege. You know that American physicians in general are quite conservative. But I am what they call a liberal, which today in US politics is suppose to be a dirty word. I think that one of the big tragedies is the fact that we are one of the most wealthy and productive countries in the world, yet 20 to 30 millions of Americans don’t have health insurance. So, if I had an opportunity of changing anything, I would change that.

**AHS** – How many times have you been in South America, and in Brazil in particular?

**MDL** – I may have visited South America about ten times, including Argentina three or four times. In have been to Brazil 6 or 7 times. This is my first time in Brasilia, but I have been several times to São Paulo, twice to Bahia, once in Porto Alegre, Florianopolis and Rio de Janeiro. I enjoy Brazil very much, and admire the people, their attitudes and their culture, and also the beautiful land. But one of the things that I have always been concerned about in South America is the problem of poverty.

**IFP** – Did you enjoy Brasilia’s architectural conception ?

**MDL** – Yes, I seem to have stepped off one airplane, into another, which of course is the shape of Brasilia (smiles). Brasilia is a very interesting and beautiful city. I had read about Brasilia, and the way it had been built, for many years, and this is the first opportunity to see it. I am very happy to be here.

**MMA**, **AHS**, **CBP** and **IFP** – Thank you very much.

**MDL** – Thank you.

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