Interview with Professor Eduardo Cazap

Latin American and Caribbean Society of Medical Oncology (SLACOM), Buenos Aires, Argentina

CANCER CONTROL

I know how busy you are, and I really appreciate the fact that you have time to do this interview. Okay, so question number one is: how long have you been in cancer?

PROFESSOR CAZAP

Well, I started my medical career here in Argentina, in 1960s. I entered to the School of Medicine in 1966. At that time, I was 17 years old. Don't worry! There is an Argentinean doctor that obtained his medical degree at the age of 19. I think that he's the youngest and he was also trained in oncology

I have some family background because my father was a medical doctor, also working here in Argentina. And he was trained as a dermatologist, but he was interested in cancer. He was partially trained at the Roffo Institute which is the oldest Cancer Institute here in Argentina. Dr Roffo was a researcher in the early 1900s and he was one of the first in the world working with the carcinogenesis of tobacco,. My father was interested also in that. His thesis was about cancers of the inferior lip in pipe smokers because of the pressure of the pipe over the lip. And that was true because it was practically all the cancers in pipe smokers were predominantly in the lower lip. Sadly, my father died at the time that I was 13, but he had time to become one of one of the very first radiotherapists in Argentina . That was in the Fifthies when radiotherapy was a very young specialty, before cobalt, and most of the equipment was teletherapy,

Well, about my career, my idea was that to be a good doctor, it was necessary to be a good clinician. So, I started: I was young, the first oncologist in Argentina having first done three years residency in internal medicine. At that time there were two or three main groups or institutions working in cancer in Argentina. The number one it was the Roffo Institute, a big institution with many doctors, but there was also a small group at the Military Central Hospital in Buenos Aires that was predominantly working in a specialty called "chemotherapists" at that time.

This group was incredibly active, it was a small group but it was like a factory of the future, producing several future leaders in Argentina. This group had a small lab doing studies of cell kinetics because at that time, the basic science behind

Talking at the World Cancer Leaders summit, 2011, Ireland

cancer was the understanding of the cell cycle, differentiation, undifferentiation and the cell cycle At that time, the knowledge about the stem cells was very, very elemental. The group had rapidly some good connections , for example with the NCI. So early in my career, I was part of the group working in a project of the NCI, a programme constituted by groups in Latin America working with partner institutions in the United States and our group was working with a new institution, the Lombardi Cancer Centre in Washington, DC.

CANCER CONTROL

So, is this now around the 1970s?

PROFESSOR CAZAP

We're talking about 1975 to 1980 now. That was about less than 10 years of my graduation. But the research at that time was at the cellular level very basic, and at the clinical level, the number of drugs were only a few. My boss, the leader of the group, Dr Roberto Estevez is considered the father of cancer chemotherapy Latin America (later on named oncology) . He published in the 1950s a book about cancer chemotherapy, similar to the Pinedo book in Europe. At the time there were, I don't remember exactly, 10 drugs?, and the book was in two volumes. Two volumes for 10 drugs! Can you imagine? But he was very enthusiastic and committed.

This was the starting times of CMF with Bonadonna's

combination. And it was curious because the first thing that we had to do on entering the group was to receive a booklet; like a guideline, but guidelines didn't exist then. The booklet consisted of chemotherapy protocols accepted for use within the Chemotherapy Service. Two leading groups – one group in the United States organized by Dr Bernard Fisher and the other Bonadonna's group in Italy – were very productive in some first chemotherapy combinations: in lymphomas and breast cancer.

It was interesting because in the booklet service there was, one very good chemotherapy combination for breast cancer, constituted by cyclophosphamide 5Fu and methotrexate. During the next two years, I remember that Bonadonna launched his historical CMF: exactly the same combination. The problem was that, at our department (which was the number one in Argentina) the publications were only in Spanish and the dissemination of that publication was only in a really limited area of some Latin American countries, so that seminal work was never included in the international literature.

By the end of the 1980s things were evolving. We were moving our group to different institutions. My boss and I founded a private Cancer Institute in Argentina. Eventually I became the director and the institution survived 20 years. Around the beginning of the 2000s the social limitations of the healthcare system in Argentina were very complicated. The survival of a cancer institution without the public support was not possible and the possibilities of development in Argentina, were not really feasible. So I spent some time at the Gustave Roussy Institute in Paris working with Jean Pierre Armand and other colleagues. I spent some time at the Lombardi Cancer Centre working with Phil Schein, and his group. We published some publications on Fluoruracil, Adriamycin and Cisplatin (FAP) for gastric cancer – which was the main tumour that was under research at Georgetown at that time . So, that was something until the decade of the 1990s.

I have completed practically 40 years of medical activities, you know.

Immediate Past President and BOD , UICC, Geneva, 2011

CANCER CONTROL
And how has the scene changed in all those years?

PROFESSOR CAZAP
At the beginning of the 1990s the cancer world was extremely limited. The idea was that cancer curability will be achieved with research. This is linked with the US vision. You can remember 1971 – that was one of the turning points in modern cancer history – when President Nixon signed the "War Against Cancer" document, with the objective of controlling or curing cancer for the year 2000.

CANCER CONTROL
I remember.

PROFESSOR CAZAP
Curability was not possible, but during those 30 years, the human knowledge about cancer increased enormously; perhaps much more than the previous 2000 years.

Curability was not achieved, but with part of the money from that programme, the governmental part of the Human Genome project was funded. So that project was successful in some important part, but not totally.

Very early in that decade I started to think that perhaps that the vision was a little bit limited and not so feasible to achieve in the next 50 years.

CANCER CONTROL
Yes.

PROFESSOR CAZAP
I realized that it was necessary to follow some different philosophy; a philosophy in which cancer diagnosis and treatment were part of a more extensive understanding and plan of action. I started with other people like Franco Cavalli and others trying to figure out how controlling cancer by different means, could be a better strategy. This is the precedent experience previous to cancer control globally, yes? So, we started with the concept of cancer control meaning that the whole world together would achieve a successful outcome. This initial concept of "global "at that time was immature, because the idea was to have global cancer control, and today that is impossible.

CANCER CONTROL
How do you mean impossible?

PROFESSOR CAZAP
The idea was that the World together would do something to improve cancer curability and control. But now, we understand

that the equation is a little bit more complex. It is a combination of developing countries, developed countries and global institutions working at the country level as well as the regional, sub regional and global levels.

The majority of the systems are country-based, so the decisions are taken country by country, whereas the great concepts and plans are regional or global. So now we understand "global cancer control" as a combination of global and country visions. So I started this conversation with my friends, majority of them from ASCO and the idea was rejected.

"No, we are Americans, we have our development and we have our institutions and we have our competitive groups."

"And what about global cancer? "

"We are Americans."

So during those decades, I had a very good interaction with the leaders of ESMO. At that time, ESMO was constituted by European countries. So I presented to the Board to have Argentina included as a member of ESMO.

"No, no", they rejected me because Argentina was not in Europe. "We are Europeans "

In the following years Israel entered ESMO and I insisted. "No, no, but Israel is not in Europe" "No, no but Argentina is in South America!" Well, finally, after many years of pressure, Argentina was the first country outside Europe to have been a member of ESMO. That was in the early times of the concept of global cancer control. I am talking about Europe and the United States because at that time they were the two leading sources of cancer as a science, with knowledge in clinical systems.

So finally, Argentina was a member and later, the position of ESMO was that it was not able to have all the Latin American countries as individual members, so the decision was to have a Latin American group working with ESMO. And then a US group was accepted.

I was always trying to convince my European and American colleagues that they should expand their organizations and to think that the world is not only Europe and the United States. And I know that today this idea is something very basic , but it was not easy to convince our colleagues. Now this is a global reality that many of the organizations are supportive, although I'm not so sure that that "globality" is clearly understood.

CANCER CONTROL

What do you think are the impediments to global cancer control?

PROFESSOR CAZAP

I think that we need to understand the players working in cancer control so that we can connect and understand the components of the issue with more clarity. At one time the world was dominated by treatments, by pharmaceutical companies and by medical associations. That was a very basic structure. We are talking in the early model of healthcare systems in which the concept of public health was for many years based mostly in hospitals , doctors, and treatments: surgery, radiotherapy or medications. All other elements of cancer control were practically absent. There was, of course, some actions on prevention, but the strategy of the early prevention measures was somehow naive and simplistic, and also limited by the knowledge that was available at that time.

We know today that the famous Papanikolaou screening test is impossible to apply to the world population. How can global cancer control face early detection and curability of cervical cancer with a test that is costly and difficult to obtain? You need a complete coverage that is not possible to obtain.

Furthermore, if a wide coverage with a proper screening methodology is feasible, you need the necessary resources in place for a timely diagnosis and a proper treatment, something frequently not available. (Similarly, with mammography; at that time, the idea was to expand the use of mammography. That is not possible under the current concept of global cancer control.) Many studies and groups were insufficient to obtain the final product: eliminate cervical cancer. That will never be achieved only with Pap smear. It is very different now with a vaccine and with other forms of early detection to simpler, more accessible and that can be widely applied. Anyway, the campaigns were successful for public education, but not for the eradication of cervical cancer.

CANCER CONTROL

That must have been a radical position to take at the time.

PROFESSOR CAZAP

For the past two decades I have been insisting that if the world has not a focus on global cancer control, and the focus continues only in diagnostics and treatment, something is going wrong. The incredible achievement of new drugs and many different new therapies today, the ones based on proteins , genetics or molecular targets or monoclonal antibodies these are more and more limiting.

CANCER CONTROL

Why limiting?

PROFESSOR CAZAP

Because the cost increases and the global access for cancer control decreases. Instead of having one drug like Adriamycin for 10 cancers, you will have one therapy for 20% of patients of one given cancer. So you have extraordinary therapies giving 70% of curability for a minority of patients. So, in the many discussions that I have with different stakeholders, the

problem is the concept. If you are trying to get an objective following a strategy that is not the proper strategy, the results will not be successful.

I think that one of the historical pillars for global cancer control was the Union for International Cancer Control. The UICC is perhaps one of the leading partners , if not THE leading organization, for the understanding of cancer as a human disease that affects all of us globally. But I am not sure if we will have so many "global" solutions, like a vaccine against cancer, we need to find the solution and have better strategies at each country level in order to use the current existing resources properly. I am not talking about new things. We need to apply much better the existing knowledge, that regrettably applies today to less than 20% of the global population.

CANCER CONTROL

The majority of research that's accessible has been done on white populations in in high-income countries. That's a very crude way of saying it, but it's true.

PROFESSOR CAZAP

Absolutely. Let's analyse my own situation. I am a man of 75 years old, and suppose that I have a prostate cancer. So my doctor gives me X. "Treatment X is fantastic for you!" he says, following guidelines from NCCN, ASCO or ESMO.

"Doctor, could you please tell me how many non-US or non-European patients are in those?"

"Could you please tell me how many patients of 75 years old are included in the studies?"

"Could you please tell me about the race and genetic background of those?"

"No, no, no".

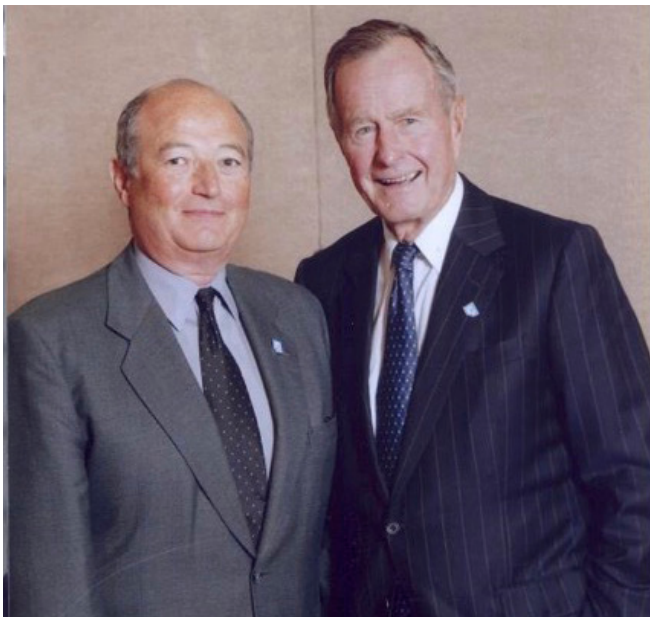
So that treatment is perfect for another person but is unknown for me. This is a methodological problem. If you do not correct the world methodology in cancer research, , evaluating which type of science we will apply for Phase 1, 2, 3 trials in drugs or other treatments, data from the literature will reflect only partially the different world populations.

CANCER CONTROL

But there is a problem there. Because companies may not want to invest in research of a drug that might benefit people have a different genetic makeup, you know, or jn a different region if that population doesn't have the money to buy the drug. Is the idea of "Well, even if we found a drug, would there be a market for it?" true? Is research market-driven or human-driven?

PROFESSOR CAZAP

We need to discuss in detail the strategy about the role of governments in the development of cancer treatments. That is



With President George W Bush, Cancer meeting, USA, @ 1991

perhaps one of the basic questions for the currently discussions about a Global Cancer Fund. The money governments invested in global health – not only in treatment, but in water pollution and many other things related with health –during the last decade was US$ 87 billion. The three main NCDs: diabetes, lung diseases and cancer received only US$ 3,000 million. This is a political issue.

Money from industry follows the objectives of the industry and that is correct, because those companies must report to the investors. But in the case of our populations, the investors are the common people, contributing with their taxes, so the government must take a leading role. But the problem is 1) political will, and 2) a good strategy, and combining those two parts in a proper way.

A good strategy includes education: it means good information, and not only education of the people but also education of the doctors, education of the political leaders, education of everybody, because cancer needs a coalition between all parts of society including pharma companies.

CANCER CONTROL

Yes, I get the impression that the politicians don't understand how serious the problem is. They took 30 years to admit climate change, and I don't think they recognize yet how, if you look globally, or even if you look by nation, how serious a threat cancer is. Either if you're a high-income country, you've already got a serious threat, or if you're a low-income country, it's coming in the next 20–30 years.

PROFESSOR CAZAP

Yes, yes. you are correct, but with some exceptions.

ASCO Distinguish Achievement Award , 2019

CANCER CONTROL
Go on.

PROFESSOR CAZAP
When the politician is personally concerned. President Dilma Rousseff in Brazil launched a nationwide programme for the prevention of breast and cervical cancer. President Chavez of Venezuela had cancer and he was interested when suffering with the disease; the father of this initiative, "the Moonshot Project" comes from the United States. Why? Because of President Biden's son, Beau. But we have an additional problem: healthy people!

CANCER CONTROL
The healthy people?

PROFESSOR CAZAP
We recently had an election here in Argentina and I was reading some of the information that was provided to the candidates for the Presidency about the priority actions requested by the people to the political leaders. They were Inflation, security, corruption at the top of the list... health and cancer were between numbers 15 and 20. We have two components to this problem: the politicians and the people. If society does not take a leading role pushing politicians to improve health, nothing will happen.

I think that many of these cancer control ideas from Latin America are applicable to all diseases in any country and globally. We have examples, the coalition in Peru against cancer was fantastic and helped a lot to realize the implementation of cancer control, the support for the National Cancer Institute, a National Cancer Plan. At the beginning of this process, the budget for cancer was obtained at the country level from the taxes on the tobacco industry; something very innovative. Of course, after successive governments with different political ideas, there was not continuity. But we have extraordinary models that we would like to share.

I would like to go back to UICC.

CANCER CONTROL
Yes, please.

PROFESSOR CAZAP
Because the UICC launched perhaps one of the very first tools for cancer care in the 1950s – late 1940s: the TNM. The TNM was the first global classification of tumours. Before TNM. cancers was not classified, so the interaction between scientists had no correct wording and a technical language for stages, metastasis (Yes or No), size of the tumour, you know. And the TNM was of course, following an idea of Professor Pierre Denoix, an excellent French surgeon who was later on President of the UICC.

Founded in 1933, the UICC is one of the oldest global cancer organizations. At that time UICC's main objective was research. But between the 1950s and the1990s, it was more involved with global treatments and TNM. Today, the TNM Committee of the UICC is still working very actively, having 70 years of leading in a common language for cancer. I am mentioning this because the evolution of the UICC is the evolution of the cancer control in the world.

When I was younger, working as a medical doctor in cancer we had in our country several UICC workshops for basic cancer or advanced cancer. These were educational programmes organized and funded by UICC before ASCO, before ESMO. The educational programmes of the UICC were fantastic, and the UICC paid for the doctors' travel and other expenses. But by the 1990s UICC was an old institution and it was necessary to change its role and its structure. I was part of that group working since the beginning of the century, and Professor Eliezer Robinson (Israel), John Seffrin (United States), Franco Cavally (Switzerland), David Hill (Australia), Mary Gospodarowicz (Canada), Tezer Kutluk (Turkey) and me, during a period of 20 years was a fantastic group of leaders, reengineering the organization. The institution today is one of the global leaders of cancer control (if not THE global leader) and has a clear mission and vision. The UICC thinks that the basic component of better cancer care, survival and curability is cancer control, not only cancer treatment.

"UICC's mission is to unite and support the cancer community to reduce the global cancer burden, to promote greater equity, and to ensure that cancer control continues to be a priority in the world health and development agenda."

One of the decisions we had to make was if should we expand the UICC or should the UICC be like a facilitator; a connector gathering together people with a common objective? And

the decision taken was the last one. Instead of expanding the UICC, the idea was to start with projects, and if the projects are useful for better cancer control – like C/Can, we would make these projects autonomous, independent, because it will be very difficult for UICC to keep their clear objectives with new areas. So, one of the very first initiatives was to improve cancer control through the collaboration with the other noncommunicable diseases issues because otherwise it would be difficult for the cancer community to obtain a global voice. In that way we presented the matter at the second High Level Meeting on Health In the history of the General Assembly of the United Nations. The first one was in 2001 on AIDS and the second one was in 2011 for NCDs.

Taking office at the UICC, Geneva, 2010

CANCER CONTROL
I remember.

PROFESSOR CAZAP
I was the Chair of the Advisory Committee to the High Level Meeting to the President of the United Nations. I thought at the time that having all these important people interested in cancer was fantastic!. One of my difficult experiences was in my first conversation with the President of the United Nations Assembly who was the Swiss Ambassador in New York. Talking with him, giving some advice about how to manage the Assembly on NCDs, it became clear to me that the Swiss ambassador had no idea about cancer. Of course, the idea of any person that you can stop in the street and ask about cancer, they will know. So that, for me was a shocking thing because If the leaders of the world have that so limited knowledge about cancer, what can we expect from the general population?

CANCER CONTROL
Exactly.

PROFESSOR CAZAP
It's the leaders of the world – can you imagine? – they had no idea. Well, a general idea. And with a general idea, you reach nothing, zero. Less than zero. That was something very shocking for me.

So after that, we got our objective: NCDs were at the top of the political agenda. What has happened today, after 13 years? Nothing. Nothing. And now, more dangerously, many governments are moving from cancer control plans to NCD plans.

CANCER CONTROL
Like the UK Government.

PROFESSOR CAZAP
Like the UK, my dear friend.

CANCER CONTROL
Yes.

PROFESSOR CAZAP
Twelve to 15 years of work for nothing.

CANCER CONTROL
Yes.

PROFESSOR CAZAP
Yes. What is the world doing in country control now?

Let's move on to take a look at Latin America. Next year we will have our first Latin America Global Cancer Week . We are setting up the website now. A few months ago we launched the Latin American Code Against Cancer, joining forces with IARC and with PAHO. So, we are active, we are trying to get real things done, we are seeing through the application of this strategy for cancer control. The Code is a tool developed 15 years after the European version. After Europe, this is the only Code that exists. And now, I think that motivated by our work , IARC has a plan for a Global Cancer Code that will include Asia Pacific, Africa and the other regions of the world, and for each region to have their own Code because the Code is fundamental. It is the basic tool for healthy people and for cancer patients, but the focus of the Code is the healthy population because today the medical objective is not only curing cancer. Today the ultimate objective in global health is to avoid diseases and for that primary and secondary prevention is fundamental.

Let's one minute think about molecular medicine. We understand the value of the new technology, genetics, molecular medicine and other new achievements. but we are planning and envisioning to use that new methodology not only to cure cancer but also for improved prevention. Let's imagine that you have a little baby girl. She is three days old. You take a drop of blood, air or saliva, you can make a genetic test and the genetic test will say "This lady has a very low risk

With Dr. Tabare Vazquez, President of Uruguay, AAOC Congress, Buenos Aires.

of having breast cancer". So that lady will have a breast cancer screening procedure every five years or 10 years. Now another girl has the highest possibility of breast cancer; that lady will be screened more often selectively. Are you with me?

CANCER CONTROL
Yes

PROFESSOR CAZAP
We need to think in a way that the new knowledge would be applied not only for treatments. We need more new innovative tools in cancer prevention and that is part of the strategy. Because if I propose to the government, "Are you okay for Argentina to have one thousand new mammographic equipment?" the politician will say "Yes". Then will be an article in the newspaper, 'The Minister of Health donating 1000…' But if I talk about something what will happen In 30, or 40 years from now? So we need to make this understandable for the politicians. If not, we are in a problem, my dear friend.

CANCER CONTROL
Thank you that is a good summary of some of the global cancer control activities that are currently happening in Latin America.

PROFESSOR CAZAP
Of course, it needs a lot of improvement. Mainly we need understanding of funding. Practically there is no funding for cancer control actions in our region. Most of the actions are based on volunteers, or fantastic ideas that I am sharing with you. But the possibility of success without money is, you know, almost impossible.

CANCER CONTROL
One of the questions I have to ask is what do people get wrong about Latin America? Or do people not think about Latin America at all?

PROFESSOR CAZAP
For me, this is a difficult question to answer, because I don't have an US or European mind.

CANCER CONTROL
Okay.

PROFESSOR CAZAP
I have a Latin American mind. Of course, my understanding is of the minds of the cancer people, not the minds of a population. The cancer people, they know about cancer in Latin America. The problem is with the general population, informed through the newspapers and media, and the people participating from as civic society players.

But I would like to say a couple of things. One, it is not relevant if the situation is Latin America, Europe, or Africa; the situation is the same. Of course, in the United States they think that they are in a different situation. Yes, in a general analysis they are in a different situation. But, let's analyse one of the 25 or 30 million uninsured people in the United States.

Let's think about the minorities in the United States…

Let's think about a family in Utah, in the middle of the mountains or in a small town.

Those are sometimes in a worse situation than in many Latin American countries.

I was invited once to a meeting that happens every year for all the cancer institutions in the United States. I was invited to give a lecture about Latin America. The meeting was, I think, two or three days long, so I attended the whole meeting to see what happened inside the United States and to better understand the internal cancer situation. There was a presentation – I don't remember the lady or the topic, – but she showed the map of the United States with the colour of each state and cancer curability. The delivery of cancer curability in some states was a disaster. Curiously, that map was one of the first times I think about Mr Trump. The map was practically superimposable with a map of the states that Trump won.

CANCER CONTROL
The Republican states.

PROFESSOR CAZAP
The same states with lower cancer curability.

So to me, from a scientific perspective, geography doesn't matter too much. The rich person in India, the rich person in Africa, they don't have any problems. They will receive care be much better than many US citizens. The problem is access. The problem is availability of resources. The problem is more socio-political than medical. The person that faces less possibilities in any part of the world is the same; in the middle of Ukraine, in the middle of a war in the Lebanon, in Haiti...

But to answer your question: I think, basically, that for the majority of the population, they are not aware of Latin America. They think that Brazil is Argentina, they think that Buenos Aires is Rio.

CANCER CONTROL
Thank you, Professor Cazap.