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I am Blake Hailey and we are pleased to have with us Dr. Harvens Lal, the Chair of the Pharmacology Department here at the University of North Texas Health Science Center at Fort Worth and we are making this video tape in the Gibson D. Lewis Library in the Biotech Communications Center. Dr. Lal I appreciate you taking time out of your extremely busy schedule to work with us today.

Blake Hailey: If we could I would like to start with your prior experience, I think you came to TCOM in 1980, perhaps you would like to go back and tell us about some of your experiences leading up to your time here at TCOM.

Dr. Lal: I came to Fort Worth from Rhode Island and let me digress a little bit. I was born in a place which is known as Pakistan it was United India at the time of my birth. Then the country was partitioned into two. In 1947 we moved to what we call Indian site. Once I was uprooted from my home town I made up my mind not to stop anywhere else until I reached the best place there is for my personal and career development and I made up my mind to come to the United States. I went to school in India and completed a Bachelor of Pharmacy degree at Benja University and move to the United States where I got my Masters at the University of Kansas in Pharmacology and Toxicology, then moved to the University of Chicago. My reason for going to the University of Chicago was that

it was an excellent University for one, but also that was the University that pioneered the use of radioactive isotopes in pharmacology research and I was very anxious to go learn their technology to apply in my future research and perhaps go to India and set-up a lab where that new technology can be used. So that was a kind of reason but turned out to be that I had a very good education at the University of Chicago where I graduated in 1962 and was hired by a place called Illinois Institute of Technology Research Institute where I immediately took over a project which was funded by the Department of Defense related to a biological warfare agents. There my job was to determine the mechanisms of action of the substances. I stayed there until 1965 when I was offered a position of Associate Professor at the University of Kansas from where I obtained my Masters Degree where I was a graduate student at one time; I took that position and I started working there until I realized that I wanted to move to a little better situation where there is a greater education and wide associate with several medical school colleges. I was offered a position to start a Pharmacology program at the University of Rhode Island and I saw this was between New York City and in Boston where the number of Medical School institutions and still I did not have to live in Boston or New York. I lived in a kind of suburban beautiful place in Rhode Island, and there we stayed until 1967. We moved there in 1967 actually and several years I worked there until I was promoted to full professorship. Then someone nominated my name at several places; one of the places was at Texas College

of Osteopathic Medicine. When I was a graduate student at the University of Chicago, I graduated and I wanted to participate in teaching which required teaching skills but the University of Chicago faculty size is very large and my Chairman told me it would take a while before my total would come to participate in medical school teaching. I looked around for other opportunities and I found a few blocks away was the Chicago College of Osteopathic Medicine. Chairman of Physiology and Pharmacology Dr. Cowsal he was known to me and I went to him and he offered me an opportunity that I could come and teach Pharmacology there on a volunteer basis; so I did that kind of on the side. I began my Pharmacology teaching at Osteopathic School at that time, so I was familiar to the school somewhat.

Blake Hailey: This was in 1967?

Dr. Lal: No this was in 1962-1963. When in the late 1970's an opportunity came up to consider to move to Texas College of Osteopathic Medicine. I was familiar with osteopathic school philosophy and I came and looked at the facilities and the plan and I thought that is the place I want to build my career because I saw an opportunity where I could start at the base level and get things accomplished which would be very enforcing for me and for the rest of my life, and that is how I accepted the position here. I came here from Rhode Island. Dr. Ruler was the President who hired me and we negotiated the position one item came up, Dr. Ruler wanted

to strengthen the Basic Sciences Department and since we were a small school his idea coincided with my idea that each department should concentrate on a particular discipline and not dilute itself and my background was in negro sciences and he said okay Pharmacology Department can develop that with Pharmacology and Nuero Sciences. After I came here, the Presidents wish that the Physiology Department develops into another competency and that was the Cardiovascular System where the strength was. The College hired Dr. Carl Jones who brought in his strength and faculty strength and developed an excellent department with the competency in coronary circulation and cardiovascular diseases. So, TCOM started with basic sciences developing different specializations and competencies in each of the basic sciences department that fitted very well in my philosophy of career development and the College Administration.

And that was how it started and my background coming to TCOM.

Blake Hailey: That is great and we are very fortunate to have you here as well.

Dr. Lal: I am very pleased as well.

Blake Hailey: Perhaps if you would, could you go into some of research you have done over the years, and the research that you are involved in currently.

Dr. Lal I think my research interest can be divided into two major categories. One is in the area of aging and the other in the area of substance abuse. In the area of aging, again there are two major efforts. I should make it a point that in Pharmacology our job is to develop new and safer drugs for treatment of various diseases; and in the area of aging are interest was what is the basis for determination of brain function.

Several years ago with the developments in neurotoxicology of brain aging, which resulted from aging, I followed up accumulation of pigments in the brain called microfistin pigments and these pigments developed in the nerve cell and in heart cells as a function of age, and I called the metabolic garbage which accumulates in the nerve cell and kind of chokes the nerve cell and it cannot perform its functions. My research started with that and moved into neuroimmunology. We found that with aging particularly in the senile aged population; there developed some antibodies that we circulated in the blood which were specific to band proteins particularly in the brain; it was very intriguing because brain is kind of immunologically protected and our immune system develop in the blood and brain is protected from them and it was kind of very intriguing why there should be antibodies circulating in the blood which was specific to proteins in the brain and perhaps producing brain damage as a function of it because they were only found in aged and they are found in mice, monkeys, humans, "Animal Kingdom". That in duress continues until today where we are in process of

collecting the presence of those antibodies with the neuropathology in aging and of some mental disfunction particularly disfunction of learning and memory; as you know with aging we being to loose our memory functions is it that it is an autoimmune disease that some of our brain proteins become anti-jointed so the body recognizes them as foreign proteins because they were not present before they were generated as a volunteer with aging with the reason that we do not know and then they start stimulating for a mission of antibodies which are trying to destroy them. We are starting those proteins in the brain and the antibodies which are circulating in the circulation and commuting down with the memory dysfunction and see if we can denucleate them.

More recently my interest in that area was developed in the free radical formation. A lot of research is coming into the literature would say that with the body functions, metabolic functions they are producing oxygen bi-products which are toxic to brain cells and all cells as a matter of fact particularly to membranes; and this toxicity is very small but it kind of accumulates over time over years. Many other damages may be caused by this mechanism so our interest has moved towards this direction there is a lot research going on but very little on the brain, a lot more notice to free radical damage done in other articles and other cells but very little is known about the brain. I think we are starting to feel that the brain is the target for study, and we have found that there are a lot of damage in brain cells which is especially to

various brain areas depending on which areas are exposed to metabolic reactions which produce free radicals and oxygen bi-products. Here our objective is to first localize where those reactions are taking place also we find that free radical damage increases with age and is correlated with neuropathology and perhaps correlated with dysfunctions or deterioration of brain functions developed with aging. As I said in the beginning the objective is to find the treatments that can retard these changes based upon aging or if they have already occurred can reverse some of the changes. In that case we have adopted two approaches, one is caloric restriction. The idea was basically that the metabolism of the calorie regenerating substance in the body would produce oxygen bi-products. We eat and we consume food, during this metabolic process the oxygen byproducts are generated, so if an individual consumed less calories and metabolized less calories, that would produce less damage. If the aging is related to the free radical damage then the longevity would increase, and as a result this does happen. Calorie restricted animals live anywhere from 20% to 100% longer than their counterpart control who were given unlimited calories to consume. We also found that many brain dead free radical mediated brain damage are retarded in those animals. In those animals there is also a retardation of the process of deterioration of memory and learning functions, so we are very excited about it. Other labs have reported that calorie restriction almost eliminates certain types of cancers in mice and in rats and research is being undertaken on hard animals at this stage. Since the

pharmacology department specialize in drugs, we are currently working on the drugs which may prevent the free radical formation and increase the productive longevity, also we are interested in the drugs which promote the health of cholinergic cells. In the brain there are cells which communicate with each other through a chemical process and there are many chemicals involved. One of the chemicals called acetylcholine is involved in many, many, brain processes and there has been data that, these cells degenerated during aging. We are studying the drugs and the chemicals which promote the health of these cells. Number 1 to reduce the rate of degeneration of these cells and also promote the health of the remaining cells so that they can better function. There is also evidence that there are substances produced in the body which inhibit memory process and there are substances that promote memory process so there is a balance of these substances. We are producing drugs and investigating them, which affect this balance in a manner, the amnesic effect of the acetylcholine is reduced or retarded so that we can live longer with our intact memory or reduce the deterioration of memory, which is a major function after we conquer the heart disease and cancer and start living longer. As the brain gives way and the memory is not there, the quality of life will be not worth living. To improve the quality of life we need to keep the brain functioning and intact. The idea of our area is in terms of the aging research. We are very excited and we are very reinforced by the results we are getting and the grant support we are getting from health and other agencies. I want to review



our substance abuse, before I came here my target of research was heroin abuse, and there I was studying the mechanism of dependence and why people become addicted to heroin. My major targets were, one; why people begin to experiment with drugs of abuse and those are a variety of reasons, but the next stage is they get hooked on the drugs, why do they get hooked on the drugs, because these drugs produce some brain changes, also their lifestyle and environment become conditions to drug taking. My emphasis was on that and I as I realized 25 years ago, produced hard data in animals, that animals can be trained to produce conditioned effects of drugs of abuse. During my study I found out that the, what was more of the time of Pavlov, that if you pair to different environments such as a dog and a food, the dog starts to producing its self salivation which would originally be produced with food, this is the pairing effect. I started doing research and got results that suggested that sometime the, many times the, conditioned effect are not like the unconditioned effect but opposite the conditioned effect and this area was developed because of pharmacology truths, for example; if an individual takes heroin it raises the body temperature, now if this heroin taking is associated with some environment, he would repeatedly, systematically, become to acquire a property of enlisting a hormone reaction in the body, an one would expect that what is happening is that when you abuse this environmental stimulus, change, the individual would feel like the individual is taking heroin, without taking heroin. That was published and we thought that, that is what is happening in terms

of relapse, people who are detoxified and then return home to there environments, where it was the same as the one they were used to inject heroin. Those environment enlisted heroin like feelings in there body and they wanted to abuse again, and that was one of the reasons for the relapses even if they were chemical free. There environments were producing drug like reaction. That led us to a logic saying how do these environmental stimuli produce a drug like reaction. One possibility is that these stimuli release the bodies own drugs. This was published in late 60's early 70's, this data, even before the endorphins and the bodies own morphines were identified. When I came to Fort Worth, one of the exciting things is Dr Still, who is considered the father of osteopathic philosophy, promoted the fact that the body produces its own medicine, but people ignored that fact. The body is a walking pharmacy and he called it "Gods pharmacy". I thought I had a tool and mechanism by which I can produce scientific data supporting those hypothesis of Dr Still, that the body has many chemicals that can be released and used by the body to treat itself, and that physicians can learn to facilitate that ability to use these medicine. That was one attraction to come to this college. That this kind of research would be more appreciated and supported, and it is supported. I already said that I started with the conditioning affect, and the other the changes in the brain produced by heroin or substances of abuse, and develop drugs which will be used to treat such substance abuse. At one time they thought you could not treat a heroin addiction because the only

substance that could stop the heroin cold turkey was the heroin like substances. I think I lab produced the first data, that you could produce non-narcotic drugs which would block the cold turkey, we published the data on a drug called Haloperidol which produced some side affects that were not desirable and the didn't use it to long. We also came up with a drug called clonidine, and that drug is still used to detoxify heroin addicts. Not only that but its use has extended to detoxify many other drugs including smoking and nicotine. In the substance abuse when I came here I concentrated on how to measure the subjective effect of drugs. One of the deficiencies in the substance abuse research was that in humans there habit was maintained because of the subjective affect of the drugs. They were taking the drug because they could produce euphoria, or a pleasant effect. They were also taking the drug because if they did not take the drug, they went into abstinence which produced a very unpleasant affect, and people were very afraid of it. They were taking the drug to avoid precipitation of that situation, but that could not be measured in animals, only humans can tell you when they are feeling good or feeling bad, and that way, it could not be measured. Our emphasis was to develop animal models that you could measure subjectively. There was a lot of debate in the scientific community about the method we propose. This is not a new thing when a new method is brought about, but now the community accepts that and close to a hundred labs across the world are using those methods that were developed here in measuring subjective affects of substance abuse, and other drugs in animals

and that was a contribution of this institution in the scientific community. I think that summarizes the two major areas of research emphasis that we have at UNTHSC pharmacology department

Blake Hailey: That definitely is a very good synopsis at that, you are also editor of Drug and Development Research of a publication, is that correct?

Dr. Lal: I, in the beginning when I started my career in pharmacology was much interested in drug discovery and drug development and I felt that the people who discovered drugs were located at the drug industry most of the time was considered most of the time the people working in the applied sciences and they were not that much respected as compared to the people who did pure science at the universities, that was not right and I wanted to provide a platform for these people to publish their data and respect it, which data may be directly geared toward the discovery of drugs. I taught to publishers and a colleague of mine, Dr. Stuart Fielding, we formed a team and started a series of books called Industrial Pharmacology. That series started to cover the drug research and discovery. Through that experience we realized that the series was not enough because the book came after a few months and the drug discovery was coming very fast. We realized that we needed to publish something on a monthly basis. We formulated a plan and were invited by several publishers. We selected aloe liss (inaudible) who was a friend of mine, he liked

the idea and said he would support it. We came up with a journals called Drug Development and Research, which was first published in 1980, that was the year I moved here. There are some questions in the mind of the publisher that, if he publishes a journal from an osteopathic college what would the image from the rest of the peer group, what would they think of it etc. I assured him that if I am going to an osteopathic institution, I made sure that scientifically there is no question, and that people are somewhat ignorant of what happens in osteopathic colleges and part of our role is established, in that we are a medical school like any other medical school in this respect of promotion of scientific research and medical sciences and I insisted that we publish the journal from this institution. The publisher went along and the journal was started in 1980. During that period, I also published my old research in many of the journals. I have close to 400 reading articles published, also the last 25 years I edited and co-edited close to 30 books and advances in pharmacology in various areas. That has been very rewarding to me, and very occupying intellectually. The journal is doing very well, I edited for it for about 13 years, and I thought that it is time for the younger generation to take over and this year I resigned from that position.

Blake Hailey: Oh, I was not aware of that, I know that looking through your CV which is very extensive, I did see several books, and was very impressed with the publishing that you have done. I

would like to if we could, move into the health science center scheme of things, and ask you about the success of the center and do you think this was the right time for TCOM to become a health science center?

Dr. Lal: Blake, this is my view of this situation. When I moved here, this place was a health science center. For the purpose of history, I still retain a pad of paper in my suitcase somewhere, where the letter head that I first used said North Texas State Univ. at that time not NTSU-HSC. That was the letter head that I used when I first came here and that was a health science center. Through the history it somewhat moved away from being a health science center and I do not know the precise reason. My interpretation now, is that the reason is to reduce the bureaucracy that came with that concept and it became a full fledged independently standing medical school. It was then realized that all medical schools were going in the direction of health science centers associated very intimately with a university. We are fortunate that we were associated with a university, and that was a very big plus. That was the reason the president has been very active in the past few years, in moving this institution toward becoming a health science center. Again I which I wont say. We are very pleased that we are a health science center. The way medical services and medical education is moving, and the promotion and development of health provider, health science professionals. It would be very difficult for a medical school to be free standing by

itself, because we are required to produce nurses, allied health scientist, public health people, and phd., teachers, researches and physician provided direct providers of health and care. They are have to be produced in one campus in one institution where they all go out with one philosophy. We cannot produce a physician with one philosophy and they go work with a physician assistant or nurses who have never heard of their philosophy. So, It is nice that the same faculty and same institution provide personal for health services at all levels. We are very pleased that we are a health science center and the institution has moved in that direction.

Blake Hailey: How do you see this particular health science center, do you see it being different from the other health science centers in the state of Texas. I know you mentioned the national picture, but how do you see it in Texas?

Dr. Lal: Well, we are the newest health science center and that is a fact, and at present we are the smallest health science center, so there is a beauty in the smallness but also it has a challenge and a lot of potential for growth which the other centers do not have at this time because they have reached their potential. We are at the right time and place, so if we are growing to grow now, we are going to grow into what is needed for today so we will be the health science center of the future, for which opportunity is if you start at this level, rather than convert something that has already been established. We are very excited that we are at the



starting point of a new health science center, which is small but it can grow under the new directions of the 21st century. That opportunity by itself is very exciting.

Blake Hailey: Do you see some other challenges that lie ahead for the health science center and you as well?

Dr. Lal: Well, our health science centers main component is Texas College of Osteopathic Medicine. That will provide a distinct philosophy of medical care. I divide the medical sciences into two categories; one, is the technology and the other the philosophy. Medical technology is the same in all the schools, the same equipment and same devices. The philosophy differs from school to school, and I think we can provide a special philosophy which again is there at the right time and place, this is the time where medicine which considers the patients human as a whole, human beings with the physicians helping the body to heal itself. To part this philosophy in physicians, perhaps in the future physician assistants and pharmacists, nurses and allied health scientists. This is an opportunity and hopefully we will direct our research in basic sciences, also which amplifies on that philosophy, so that is a very exciting opportunity for us and this health science center. The future lies in many many things, I think we are at the brink of making teaching innovations, teaching tools are changing, computer technology is changing, with virtual reality starting to be used. Instructions can be individualized to the persons potential. Our



administration is pushing to develop centers and institutions, as I mentioned earlier we as a department specialize in certain areas and we are very successful. Now , the time has come where interdepartmental cooperation increases so that we work on projects and get the project grants, we do not have any project grants at this center at this time. Project grant and centers require several departments to interact together. Dean Cohen is very much pushing and very timely pushing that we talk to each other in a more interactive way and develop a center, that is why the institution has become a center. That is the challenge to establish them, and get them funded. The technology development is very very new for this institution. Dr Gracy, associate dean for the basic sciences and research is pushing that this year and that is something new that I feel the United States of America is currently in the leading edge of biotechnology development. There are many things that have been developed here and taken over by other countries , japan has taken over a lot of technology. In biotechnology we are still the leader and will remain the leader for a long time to come. Also, biotechnology brings and produces money that can be used for research and instructional programs. The idea is to packet the research innovations of the faculty here into packages that can then be sold, in order to generate money for more research for those areas and other areas. That is a big challenge. We are going into an area of microbiology; for example, my department has been most of the time until recently exclusively a whole animal research area, behavior researcher, and we are now changing our

resources toward being a microbiology unit because that is where a lot of development is occurring presently. A lot of break through with the current research and we want to be part of it, and that is the challenge for me at this college to take the pharmacology department to the next century.

Blake Hailey: Then you do see your role as chair of pharmacology changing somewhat in the next few years, based on what you just mentioned.

Dr. Lal: My role is changing in a sense that the innovations are changing. When I first came here other colleges did not have computer aided instruction. We pioneered and we still have computer assisted instruction, and now many medical schools use computer assisted instruction. Now we want to go to the next step and develop more computer technology and develop more use for teaching purposes. That is in the instruction field. My role in the department of research, we did really well. I think we are a highly funded department even on the national level. We are the top third medical school with respect of the funding information from the institution of health, with respect to the number of faculty and the funding grants that we have. We have people in the study sections that are highly recognized by their peer group. Then my role is now that I must move the department to the next step which is combining the whole animal research with the microbiology. We made a beginning there and are going in that direction. That is a

new challenge for me and I feel that if the new challenges are not there, persons become less cooperative and less effective. Instead of living on the past glory, we must have new challenges every year of every 5 years, to remain very productive and active. I have enough new challenges carved out for me.

Blake Hailey: Definitely, you have quite a bit of vision, it sounds like into the future. Dr. Lal we have definitely covered a lot of territory here today. I want to ask now if there is anything in my lay mans line of questioning, that I have missed that you would like to go into.

Dr. Lal: I think I covered most of the things. I feel on a personal not that we are very happy, me and my family, that we move to fort Worth. I am very pleased that we gathered the faculty that are so friendly not only in their own department. We have very close ties both on the personal levels and scientific level with the other departments. Administration is very supportive of the sculpturing of the college and moving the college into the next century. The state of Texas is very generous in terms of supporting us. There are problem of a growing institution, and we need to struggle every day, but looking at other places and other people, I am very satisfied with my life and the environments, and what is happening at this center.

Blake Hailey: Well, the UNTHSC is definitely a much better place

having you here. I very much appreciate you taking the time out of your busy schedule to cover these topics with as much ground as you have. I want to thank you. I know that this will be very helpful to us later on. Thank you for your time.

Dr. Lal: Thank you for the opportunity. It was nice talking to you.

Blake Hailey: With that we will wrap today up. Thanks again Dr. Lal and hope to talk with you again soon.