Interview: Dr. Arnauld Nicogossian

NASA studies the parallels between space flight and aging

On Jan. 16, NASA Administrator Dan Goldin announced that former astronaut Sen. John Glenn (D-Ohio) had been approved to fly on a nine-day Space Shuttle mission in October. Glenn, who will be 77 at the time of the mission, was the first American to orbit the Earth, 36 years ago.

Dr. Arnauld E. Nicogossian is NASA Associate Administrator for Life and Microgravity Sciences and Applications, and is also the space agency's Chief Medical Officer. He has been with NASA for 25 years, starting out as a researcher in cardiopulmonary, or heart-lung disease, at the Johnson Space Center. He worked on the last Apollo mission, Skylab, and then was flight surgeon for the Apollo-Soyuz flight with the Soviet Union in 1975. At NASA headquarters in Washington, Dr. Nicogossian has developed medical standards and policies and procedures to select people for space flight. He earned a medical degree from Teheran University, and a Master of Science degree from Ohio State University. He was interviewed on Feb. 3 by Marsha Freeman.

EIR: On Jan. 16, NASA announced that Senator Glenn will be flying on a Space Shuttle mission this October at the age of 77. One of the experiments he will participate in will be cosponsored by the National Institute of Aging, and one would think that all of the data from his flight will be of interest for research in aging. What are the areas that NASA and NIA have been interested in working on jointly?

Nicogossian: First of all, it's a nine-day mission, so, on such a short mission, you have to be very careful about what experiments you select, because you want to measure some influence [of microgravity] and have some results.

We had two workshops with the National Institute of Aging, NIA, and Senator Glenn was instrumental in pushing forward a third workshop with NASA and the NIA, last summer. In September, we signed an agreement with the National Institute of Aging that says we will jointly continue to use space flight to draw parallels between physiological responses in spaceflight, and aging. We talk of parallels because there are similarities, but it's in manifestations, not necessarily in outcomes, because the effects of space flight are reversible after flight, and the aging process is not.

NASA aging research is relevant to areas that NIA is going to look at, including, for example, a loss of ability for exercise because of deconditioning, loss of strength, bone loss, balance disorders, sleep disturbances, cardiovascular deconditioning, as it relates to inability to have an upright posture after flight, and immune response.

EIR: Why are these areas of interest for joint work?

Nicogossian: NASA is interested because it's related to space flight, and it's applicable to the National Institutes of Health, to look at these areas to see if they present a parallel with aging processes. If there is a parallel, it will demonstrate that adaptation during space flight can be used as an accelerated model of aging, a reversible accelerated model, that one can use to study some those manifestations.

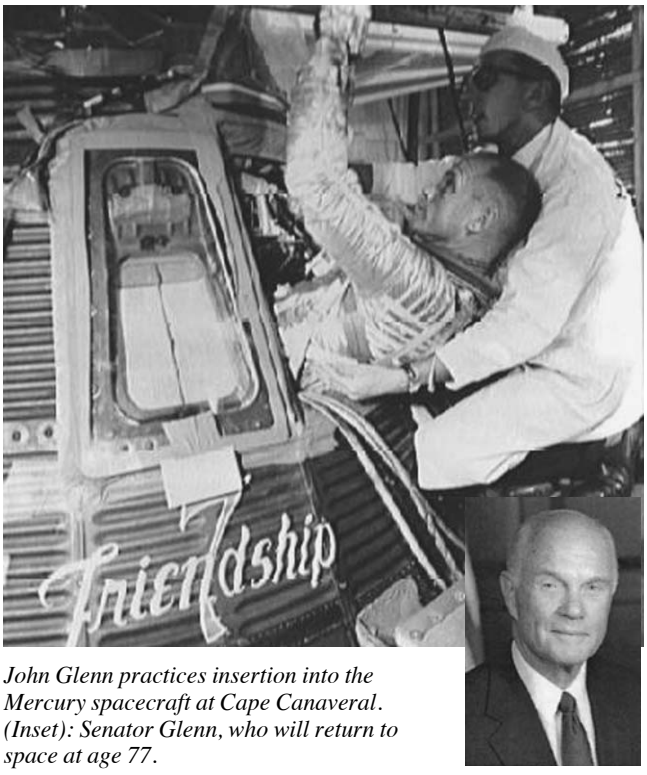
Now, what is aging? Aging has a very different underpinning than space flight. If you go to the issue of the changes created by space flight and the processes in aging, they are entirely different.

In aging, there are changes in signals in the body which result primarily in changes in the body's response to environmental stresses. In space flight, it is a change in the environmental stresses, and there is a change in the physiological response, called adaptation. Aging is not an adaptation, as far as I know, to the environment. Aging is a response of an organism which makes it unable to cope with the environment.

That is, in aging the most prominent thing that we see is the immunological inability to fight diseases. It gets attenuated. For example, elderly people are like young children, in that they are more susceptible to all kinds of diseases. Drug interactions are different in older patients: They need smaller doses of drugs, just like younger people, who need a lesser amoung of drugs and medication. Chronic diseases like arthritis and degenerative diseases of the bone and joint are more common in elderly people, including cancer, because of changes in autoimmune, or immune system response, apparent in aging. That is not truly demonstrated in space flight.

So, I want to impress on you that we are looking at the list of things I mentioned—bone loss, muscle loss, muscle strength loss, maybe immune loss in space flight, the loss of the ability to stand up upright post flight, which shows parallels in those areas.

It's a short mission, and the things that we decided we'll focus on, which are measurable and experimentally compa-



John Glenn practices insertion into the Mercury spacecraft at Cape Canaveral. (Inset): Senator Glenn, who will return to space at age 77.

tible with the short mission, were two things, that are already available in our funded peer-reviewed research: sleep disturbances and muscle protein turnover, or metabolism, if you wish.

A lot of Americans do suffer from sleep disorder—about one-third of adult Americans. There is a certain percentage who are "healthy," and they suffer because of environmental exposure such as noise; a shift of work-day cycles, when you have workers who change between day and night shift; or people who travel, jet lag. Those are environmentally induced changes in sleep patterns. In those people, you have the quantity of sleep which is disrupted. In other words, they don't go to sleep, they cannot sleep, and so on.

In elderly people, it's a different story. The quantity of sleep is not affected. A lot of elderly people usually do sleep, but the generic observation is that the quality of sleep is not as good. It could be due to changes in the production of melatonin or hormones, or the immune system. Or, the inner clock does not provide for enough rest, and that is why they are always tired.

So you have to be very careful when you generalize from environmental agents, to those that are age-related, versus disease-related. There are a lot of people who are obese and have what we call sleep abnia, and once they lose weight, they feel better. Sleep abnia is a problem in a mechanical process. They do not sleep very well. A lot of people who snore wake up because they are snoring. A lot of them have sinus or other medical problems which produce sleep defects. Other folks wake up in the middle of the night, especially males, when they have prostate problems, to go to the bathroom, and this disrupts their sleep. You have to be very careful how you quantify sleep.

EIR: Has it been conclusively demonstrated that one of the reasons for sleep disturbance in the elderly is a reduced production of melatonin?

Nicogossian: That's one of the objects of the general studies, not only in space flight, but the general studies that Dr. Charles Czeisler [at Harvard Medical School] and others are doing. They are looking in the general population to see if the time of your hormone secretion is changed because of immunological problems, creating problems with sleeping in *healthy* elderly people.

We have a different problem in NASA. The reason why we selected that experiment is not really entirely because of aging. Yes, it has an applicability to aging, but NASA has a problem of its own, when we fly to high inclinations, to the Mir space station. We have to adjust the Shuttle crew rapidly, in a very short period of time, to put them on the schedule that Mir is on, which is Moscow time, or about nine hours different than we are. Then we have to shift them back to the Kennedy Space Center time when they land.

EIR: Similar to jet lag?

Nicogossian: Yes, but we shift them through with bright lights and things like that, adaptation devices that Dr. Czeisler has developed. The reason we shift them is because during the docking [of the Shuttle with the Mir], both crews have to be awake so they can think on their day schedule. We shift both the Mir and the Shuttle crews so they can be on the same work schedule and can do the work together. So, NASA has its own problems with different orbits in space and the way we adapt to those orbits.

The way different medications are used will be one of the things that will be tested on this flight, which is part of the global research on melatonin that Dr. Czeisler is doing. One goal is to find out how much melatonin, if any, is necessary to induce sleep, or how much melatonin is detrimental to sleep, and what the relationship is of melatonin and sleep. We know that large doses of melatonin can disrupt sleep, and only very small doses of melatonin *might* induce sleep. It is difficult because there is no data. As you know, melatonin is available over the counter.

EIR: You are saying that because it is an over-the-counter medication, millions of people take it, but their response is not tracked or recorded?

Nicogossian: That's correct. It's like the aspirin study. Until very controlled aspirin studies were done with people with heart disease, using controls, the physicians would not prescribe it to prevent stroke or heart attacks. It's the same situation that we have here.

EIR: In your book, *Space Physiology and Medicine,* you

report on a study that revealed that 30% of 58 Space Shuttle astronauts stated in their debriefings that they took a medication to help them sleep in space, although they did not use any sleep aid on Earth.

Nicogossian: That information is anecdotal. There are many people who are conducting research in sleep, on other missions. It seems that, anecdotally, it was reported by a large number of people that during space flight, the amount of time that they needed to sleep decreased with the length of the period of being in space. Specifically, the Russians have reported that. We are trying to quantify that type of activity.

EIR: I also looked at the Skylab data, which was a small sample, but it seemed that sleep disturbances diminished over time, which would mean that it was an adaptation to external stimuli that caused the disturbance rather than something inherent to microgravity. Do you have any evidence that weightlessness produces changes that interrupt sleep?

Nicogossian: We think it might, we are not sure. That's why we are doing the experiment.

EIR: My impression was that the experiment was aimed more at trying to help find a treatment for sleep disturbance in space flight, rather than the causes.

Nicogossian: Remember, the experiment is composed of several things. It will measure the quality of sleep, quantity of sleep, and activity during daytime. We are measuring all of those things. And then we will be administering the medication, but it will take a long time to collect the data, because you have to have a placebo versus the medication effect. We will measure parameters of alertness and quality of sleep. There will be objective measurements, as opposed to subjective measurements. That is part of the sampling that will be started on the Neurolab Space Shuttle flight [in April]. Some of the precursor experiments were conducted on the Space Shuttle Life and Microgravity I mission, and such questions have been considered through the Mir flights, in some shape or form. But this is the most comprehensive evaluation which will be conducted. These experiments will be continued until we get an adequate sample size, which is probably between 6 and 12 people in space. Then we will have some data that we can comfortably analyze.

EIR: Have there been any experiments where you have administered melatonin to the crew?

Nicogossian: No. We are going to try it. Senator Glenn's flight is a continuation of the experiment that is on Neurolab. That's where the same experiment by Dr. Czeisler will be conducted.

EIR: Will that experiment also administer melatonin to the crew?

Nicogossian: Yes. We are also interested in the range of age, and we will have to get additional data in the future. . . . We have to understand the effects of gender and age. We fly multicultural, diverse crews in space. Senator Glenn will be 16 years older than anyone we have flown before. We have flown eight people on 13 missions who were 55 years or older, and the oldest commander who landed the Shuttle was 50, and the oldest person, a mission specialist, who did an extravehicular activity was 61. It is arbitrary to say 55 and older, but that is what is in the database.

So, if the opportunity presents itself, and if it makes sense, we are going to collect the data, and the reason why it is important to us, is to establish the experimental diversity of response of the people who are going to fly in space.

EIR: We have now had a half-dozen astronauts on the Mir for long missions. Were there sleep disturbances or disorders reported from them?

Nicogossian: Once we finish flights on the Mir space station, we are going to put all of the data together and this will be available for the public. I don't have the individual data. Yes, we have been distributing a questionnaire asking about the quality and quantity of sleep, which is similar to what we did on the Life and Microgravity Science (LMS) Shuttle mission, and similar to what we are going to do on Neurolab.

On Skylab, we measured sleep quality. On LMS, we measured sleep quality using electrodes and things like that. On Neurolab, we are going to do the same thing. We are going to obtain questionnaires, which is subjective, and we are going to obtain objective data, and put that together with age, gender, length of flight, and all of that, starting with Skylab. It will be an integrated package which we are going to analyze. We will interpret the data, to help us decide what to do, later on.

EIR: The second area of life science experiments on Senator Glenn's Shuttle mission will deal with muscle wasting in space. What will that experiment consist of?

Nicogossian: We know that once you enter space flight, there are rapid changes even on the histomorphic level, at the cellular level, if you wish, in certain areas, such as muscles and bones. They are the same, except that the muscle [deterioration] is more rapid, and you find that even on a short-duration, nine-day mission, you have reduced strength of the muscles.

So, we are trying to accumulate information on the way protein metabolism proceeds, how the proteins are assimilated by the muscle, the protein synthesis, how the muscles are built. We are trying to establish the parallels between elderly people and the problems of space flight. We think that the synthesis of proteins does not proceed the same way in space as on the ground. The assimilation of the proteins in the muscle does not happen.

One of the major proteins, which is alanine, will be labelled with Nitrogen-15, and given to the crew members before and after flight, and during the flight. It's a tracer which is a stable isotope, not radioactive, but can be traced in the urine, and through MRI, and we can measure how much of it has been utilized. We want to see the turnover of the protein,

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how the muscle assimilates or synthesizes proteins.

EIR: What do you think causes muscle wasting in the astronauts?
Nicogossian: The animal studies that we have show that protein is not synthesized very well in space flight. And if I were to extrapolate to humans, I would say the same thing happens, because there is muscle wasting.

EIR: Is disuse one of the factors, in that less muscle strength is needed in microgravity?
Nicogossian: It's more than that. There are a couple of possibilities that are open. We think that part of what is not functioning are the signals which come from the nervous system to the muscle, that they are affected, contributing to a lack of signals to assimilate the muscle proteins.

EIR: And is there a similar process in the elderly?
Nicogossian: We are trying to establish the parallels between aging and space flight. In the elderly, it is also a problem of muscle protein synthesis, and that is what we are looking for.

EIR: Is the problem the breakdown of muscle that already exists, or the fact that new muscle tissue is not produced?
Nicogossian: We have evidence that the matrix breaks, but we have not quantified which components [are affected]. Our research is also based on ground-based studies and supplemented with research done on animals in microgravity. Humans beings are one of the species that we study, and we need to do multi-species experiments. Some of the experiments were done on primates, if you recall, on the Biosatellite, and all that data will be pulled together and looked at. We will not have that many human space subjects, but if it is corroborated with the same findings in other species, then the findings become very important.

EIR: Bone demineralization during space flight is of great interest, with parallels to the aging process, which can result in osteoporosis. Will that be measured?
Nicogossian: This Shuttle mission is too short to do bone studies. We selected things which were in the peer-reviewed process already, and those experiments that are compatible with this mission.

EIR: Were the experiments chosen before Senator Glenn was approved for the flight?
Nicogossian: Yes. The experiment that was chosen before Senator Glenn was, was the sleep experiment. We were going to do it anyhow. The muscle expriment, we added, and there is another set of agreements we are now engaged in discussions on, with the Baltimore aging study, which is supported by NIA. They are very interested in looking at the pre- and post-flight data to make it part of their study, so we are looking at the cardiovascular and neurovestibular data that we are collecting. They are looking at these data and using them as part of their cohort study of aging people to see if we can establish a cross-fertilization in the kind of diagnostic tools that we use post-flight and what they can use in the elderly aging studies. There will be much more evaluation as far as orthostatic intolerance, or the inability to stand upright after landing, to maintain balance, heart function, which will be done on all crew members, as part of our pre- and post-flight pratice.

EIR: Soon you will have data for months at a time, when the International Space Station is in operation. Are you working with the NIA to design experiments that can run for three months?
Nicogossian: We work by the announcement of opportunities, and the investigator-initiated research, based on the call for experiments that we initiate. We have two main goals: one to contribute to the science, and one to contribute to health.

To contribute to the health of people on Earth or in space, are two different things. On Earth, we have the National Institutes of Health. In space, obviously their help is very much appreciated. We have also created the National Space Biomedical Research Institute, led by a consortium of universities, led by Baylor College of Medicine, which is focussing primarily on counter-measures [to space adaptation] and will be working with NIH looking at each component, such as bone loss and muscle loss for long-duration missions. We are going to continue to do peer-reviewed research, through announcements. Some of those might be focussed, some might not. Each announcement will establish our interest, and in some cases, like Neurolab, which will study the nervous system, and has significant impact on whatever we do in flight, along with things we are going to do on the ground, that type of research has been peer-reviewed by NIH. They help us to

access the broader [scientific] community. They also help us to access the data that we can use, in return, for keeping our astronauts healthy. But, we try to maintain our mission independently, and we also try to merge and use synergism with them. Research can be acquired through many sources, but it is all peer-reviewed.

EIR: One aspect of the space environment which has been described as possibly accelerating the aging process has been radiation. Are there plans to do studies on the effect of the radiation in space on the aging of tissue?
Nicogossian: The emphasis on this mission is not radiation. That is a separate program. We are looking at radiation in the context of ground-based research. We have been doing radiation dosimetry on Mir. We have been exposing different tissues and trying to establish the risk of radiation.

In the International Space Station, with the centrifuge, we are going to look at the connection, or synergy, between radiation and microgravity, or lack of synergy. We have a special program which includes routinely measuring the radiation dose on every mission. We do work with the National Cancer Institute, and we do work with the Department of Energy in radiation research, as it affects human health.

EIR: Which do you think will be the most fruitful area of medical research using this unique environment of space?
Nicogossian: The issue here is to establish or demonstrate the parallels between space flight and aging, and see if space flight can be used as a tool to study some of the manifestations or some of the symptoms of aging, in an accelerated mode, without spending years on Earth to do observations. And humans may not be the species of choice to conduct the studies. They can use genetically engineered mice, or cell cultures, or microbes, because people are starting to look for genetic reasons for turning on and off the mechanisms that are responsible for the aging process, notably for cell death. If the cells do not die at all, you get cancer. If the cells die at an accelerated rate, you might get wasting and aging, where no new cells are produced and more cells die. That is only a gross view.

If there are some parallels, if they are demonstrated, then the utility of these parallels could be a useful model and tool for study. Then, special experiments with special markers, with special subjects, which might not be humans, probably not entirely, will be developed, for NIH to do them. At this point, we always fly two or three experiments for NIH in the area of cancer or other fields, every year, because they are a priority for small experiments on the middeck on the Shuttle.

I do not know what specific future experiments will be. This is the beginning of the program, when we are going to go and look at those things, in a deliberate fashion, to see if space can help as another tool to study aging. But it is not necessarily with humans.

EIR: Have you found any difference in readaptation after a space flight, among all the astronauts who have flown, in terms of their age? You mentioned that there have been eight American astronauts over the age of 55 to fly in space, so far. Will it take longer for someone 77 years old to regain preflight measurements of bone density, and other factors? Do you think someone that age will recover competely?
Nicogossian: First, you have to describe what "all the astronauts" means. The median age of the astronauts is in the neighborhood of 38 years old. We decided that we can call anybody over 55 a senior astronaut. That is arbitrary, because we don't have an age cut-off. We have flown eight people over 55.

In terms of Senator Glenn, he can do better, or he can do worse, or there can be no change at all, compared to the other senior astronauts. As far as rehabilitation, we have not flown anyone over 55 on long-duration missions. In short-duration missions, would it take longer? We will follow John Glenn and his crew much longer [than usual], to try to find out.

NIA and people in the Baltimore aging study really want us to continue to follow the crew for 30 days [after landing], to make sure we have all the data. And we will continue to follow all of the crew members, not only Senator Glenn, for a longer period of time. I can't tell you how he is going to fare at this point. I usually am pretty good at predicting, but this time, I can't.

I bet you he will do okay, the same as the others. But don't quote me, because I cannot tell you!

EIR: Do you think there is any age limit for space missions?
Nicogossian: It depends upon how long the mission is. There is a limit on how long people live. I don't know of anybody who has lived more than 120 years, except for Abraham, maybe. There is an age limit. If you send somebody on a four-year voyage to Mars, we will consider age as a risk factor. If you send somebody for nine days or four months, we might not. There is never any other risk than age itself, because age you don't turn back, and age deals with natural life expectancy. When you say, "What can a 77-year-old or 80-year-old do?," I can tell you I can name famous surgeons who are older than that and continue to do surgery. Age, per se, doesn't have to do with anything, but it is just that age is a risk, by itself, because it deals with life expectancy.

Is it sure that we can say that a 60-year-old person will live another 17 years? Yes, the average is about 20 years, but there are others out there who can live another 40 years. What is the risk? It depends on what their physiological health is. If they are free of risk, they will live to the full life expectancy, but you cannot tell their life expectancy exactly. Would we put an age limit to long-duration missions? Obviously, you will tend to send people who are younger, because you expect them to stay for a longer period of time in space. If you are going on a five-year voyage, you will send somebody in their early 40s.