

Nutritionals Nutraceuticals Functional Foods Dietary Supplements

# NuFFooDS

perspectives on science & business  
**Spectrum**

Volume 1 | Issue 5 | April 2014 | ₹100

[www.nuffoodsspectrum.in](http://www.nuffoodsspectrum.in)

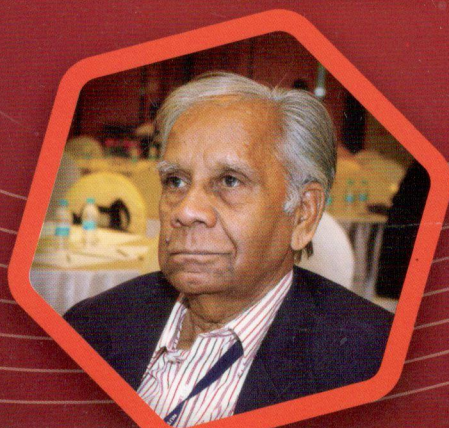
68 pages including cover

## SALUTING NUTRA LEADERS



CEO Summit

**Challenges  
of innovation**





## Dr Ancel Benjamin Keys Monsieur Cholesterol

Dr Keys, who concentrated on preventing cardiology vascular disease rather than curing it, time and again, was criticised by various commercial interests

**D**r Ancel Benjamin Keys was the first driven interventionist in the field of preventive cardiology. Ten years back, on his death, the tributes paid to him by leaders of the medical world, professional media and his academic colleagues bespeak of the several fields he had pioneered during a long and very active career. "He was a giant in the field of nutrition in a variety of ways," said Walter C Willett, chairman of the nutrition department at the Harvard School of Public Health.

Our perspective on Dr Keys is not just to enumerate his widely acclaimed contributions on: saturated fat as a primary cause of atherosclerosis (the Seven Countries Study), high altitude human physiology, formulation of K-rations for the American soldiers in World War II, the Minnesota starvation experiment or the benefits shown of the Mediterranean diet.

Of course these are very important. But we would like to understand how Dr Ancel and Dr Margaret Keys searched for the keys to some of the locked up secrets of good health and longevity. An attempt to grasp how this couple's minds worked in unison, with perseverance and future-creating perspicacity would be a story that would enthuse and inspire the young generation to explore the cur-



rent challenges in the field of lifestyle disorders.

### Research contributions

Dr Keys, who had humble beginning, studied Economics and Political Science to get his BA in 1925 and later in 1928 he got MS in Zoology. After graduation, he worked as a management trainee at Woolworth's. His love for science and research brought him to Scripps Institute of Oceanography with a scholarship. He received a PhD in 1930 in Oceanography and Biology.

Dr Keys, in his fish research, used regressions to the estimation of weight of the fish from their length. This

was a foundation in biostatistics that helped much in his latter epidemiology work. In the fields of obesity and metabolic disorders a robust knowledge of biostatistics is essential.

For his postdoctoral fellowship, he travelled to Copenhagen under August Krogh. Krogh was a pioneer in gas exchanges in respiration. In 1920 Krogh was awarded the Nobel for his work on capillaries and gas exchange. Krogh was student of Christian Bohr – father of the famous Niels Bohr. It is not known whether Dr Keys had any interaction with Niels Bohr. These sort of trans-discipline interactions have deep impact on young minds, expanding their horizons. The laboratory was small and the restless mind of young Ancel was in search of a more challenging milieu. After this fellowship, he went to Cambridge.

Dr Keys wrote, "It was fairly common in those days to move around a lot. Not so much nowadays, perhaps, but it used to be — shopping around from one school to the other as a postdoctoral fellow. If you had the wherewithal to hold body and soul together, that's what you did. I was just about to accept a permanent job at Cambridge, however, I got a cable from Harvard. So I said to myself, 'Okay, go to Harvard and see what's happening in the States.' I taught



biochemistry at Harvard and stayed there for three years." He returned to Cambridge and earned a second PhD in physiology (1936).

Later Dr Keys wrote about his job offer at the Mayo Foundation in Rochester. "They offered me twice my miserable salary at Harvard and an opportunity to set up a new division of biochemical research on human beings, human physiology and biochemistry. But after I'd been there a year I found it a little confining. With my background, it just seemed to me awfully provincial, if you don't mind my say-

the Journal of the American Medical Association for many years. We had an awful time getting him down. He was not blue but black — gas pain, retching. We thought he was going to die. You see, Brian and I had the advantage of having lived at 10,000 feet for a couple of months beforehand."

The temperature was -50° c at 20,000 feet. Dr Keys wrote, "We had expected to go to the Himalayan region in Asia at latitude of 25 or 30 degrees north. Instead we ended up being 22 degrees south in July, which is the middle of winter". This work changed the

World War II affected the nutrition of millions of civilians across the globe. He designed the classic Minnesota Semi-Starvation Experiment.

The objective of the study was to test the impact of starvation and the methods of nutritional rehabilitation. The diet was designed to duplicate that of the occupied countries of Europe — root vegetables, bread and simple starchy food. In addition the volunteers had to walk 22 miles/day. As the emaciation ensued, depression, irritability, loss of libido, fatigue and perpetual hunger set in. Remarkable changes occurred in the metabolic and cardiovascular markers.

The greatest deterioration was seen in those who were most fit initially. The volunteers needed a caloric intake of 4000 kCals in the rehabilitation phase for several months to build on their wasted tissues. The fat deposition came up first and the muscle building needed much exercise in addition to high proteins.

In 1950, the study was published titled 'The Biology of Human Starvation' — a classic even today. Dr Keys said, "Starved people cannot be taught democracy. To talk about the will of the people when you aren't feeding them is perfect hogwash." How much relevant this is for India!

Dr Keys had an early suspicion that fat produces high blood cholesterol. He examined a Wisconsin dairy farmer. "He had big knobs on his elbows and over his eyes, and when you opened them, it was just pure cholesterol inside. They had tried various things at Madison, including giving him thyroid extract to a point where he was shaking all the time. We checked this fellow's serum cholesterol level, and the first reading was 1,000. His brother, who came with him, had a reading of 600. The average level in the United States is about 220 or 230, so of course this was sky high. So we put them over in the laboratory, fed them



ing so. All the docs talked nothing but doc business and the evenings were devoted to bridge."

It was a blessing that he hired Margaret Haney as a chemistry technician, whom he married in 1939. She was his research collaborator, co-author and co-traveler for life. He joined John Barcroft's Fatigue Laboratory at the Harvard University.

In a landmark study the effects of high altitude, in Andes, on human body were shown on oxygen carrying capacity of the blood and body's ability to adapt. Two volunteers were serious. Keys wrote, "One of them was John Talbott, who later was editor of

attitude of the science establishment and the US War Department towards Dr Keys. At the age of 29, he had finally found his true passion; research in human physiology.

At the University of Minnesota he was invited to develop and test food ration for paratroopers. The aim was to develop compact nutritious food packets that could fit into a soldier's pocket. The army was so delighted with the results that eventually all the soldiers in the war received 'K-ration' boxes named in honour of its founder. He also conducted human nutrition studies with vitamin supplements with placebo-controls in early forties.



## Pioneer

there for a week, and bang! Their cholesterol levels dropped down to 500 and 300. Essentially we put them on a fat-free diet. It wasn't very tasty."

The quote emphasises the need not to forget the importance of single case studies in human nutrition under the glamour of randomised double-blind placebo-controlled trials!

In the post-war Europe, there was a drop in the prevalence in heart attacks in populations deprived of high fat diet. Dr Keys also watched the new outbreak of heart attacks in obese affluent middle-aged businessmen. He hypothesised dietary fats, particularly saturated fats having a role in clogging coronary arteries. He followed a group of 283 middle-aged (45 to 55 years) businessmen for a period of 40 years. He found that men with cholesterol level above 260 mg/dl were at a higher risk of suffering from heart attack than those with levels below 200 mg/dl.

In 1951, Dr Keys, on a sabbatical at the Oxford, heard from an Italian colleague about the low incidence of heart diseases in that region. Dr Keys moved to Naples and set up a portable laboratory.

The population showed low levels of blood cholesterol. The low prevalence of CAD too was verified. The diet had a high consumption of pulses, legumes, whole cereals, fruits and vegetables, a moderate consumption of fish, dairy products, red wine and a low consumption red meat. The main source of fat was from vegetable sources like olive oil.

He concluded that the Mediterranean style diet which was low in saturated fats and high in monounsaturated fats was responsible for reduction in incidence of heart diseases. Keys,



like other pioneers, was challenged for these findings at an international WHO meeting by several eminent physiologists. They found a lack of evidence. The young investigators should never get disheartened by the ridicule of the seniors, when their new data is shifting a paradigm.

Dr Keys designed, in 1958, the now famous Seven Countries study, with 12,763 men (40-59 years) as cohorts in Italy, the Greek islands, Yugoslavia, the Netherlands, Finland, Japan and the United States. The study lasted more than 50 years. The rest is history!

The study confirmed that cholesterol, obesity, lack of exercise and cigarette smoking increased the risk of heart disease. The fact that heart attacks were preventable became big news across the world. Dr Henry Blackburn, successor of Dr Keys said: "The Seven Countries study demonstrated the preventability of heart attacks. They were not a natural aging phenom-

enon, or genetically predetermined or acts of God."

Dr Keys wrote, "There's a little hotel in Brussels that my wife and I stop at now and then, and every time I go in there the maid, a lady in her sixties, says, 'Ah, Monsieur Cholesterol!'"

In 1954 Dr Keys, with help from Paul Dudley White - the great cardiologist, initiated more serious study of cardiovascular epidemiology. As Keys concentrated on preventing cardiovascular disease rather than curing it, time and again he was criticised by various commercial interests, particularly by the meat and dairy industries.

Dr Keys said, "There'll always be commercial interests involved in matters like this, but most of their arguments have gone by the wayside. The important

thing is to make people aware of the dangers." With the massive propaganda of food and beverage industries, the task of advocacy for healthy foods and lifestyles has become uphill, even for the developing countries.

When on his 100th birthday, Dr Keys was asked whether his diet had contributed to his long life, the quintessential scientist answered, "Very likely, but no proof." Dr Keys died two months before his 101<sup>st</sup> birthday and he was actively working till he was 97 years old.

His great message for medicine in general and cardiology in particular was, "Find out before people get sick why they get sick." **NS**

**Dr Ashok D B Vaidya**

Research Director, Kasturba Health Society Medical Research Centre, ICMR Advanced Centre for Reverse Pharmacology in Traditional Medicine, Mumbai

(With inputs from **Hiteshi Dhami-Shah**, Clinical Dietitian and Research Fellow, Kasturba Health Society - Medical Research Centre, Mumbai)